Université de Montréal

Exposition des travailleurs du recyclage électronique à des ignifuges et association à des effets endocriniens.

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Exposition des travailleurs du recyclage électronique à des ignifuges et association à des effets endocriniens.

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Résumé

Les ignifuges sont ajoutés à divers produits afin de les rendre conformes aux normes d'inflammabilité. Les plus communs sont les polybromodiphényléthers (PBDE) et les esters d'organophosphorés (OPE), qui sont détectés en forte proportion dans la population générale. Quelques industries, comme celle du recyclage électronique, peuvent exposer les travailleurs à des niveaux élevés de ces ignifuges, dont certains sont soupçonnés d'être des perturbateurs endocriniens. L'objectif de cette thèse était d'évaluer l'exposition à des ignifuges chez les travailleurs et d'étudier les effets endocriniens associés.

Trois types de données ont été utilisés. D'abord, deux bases de données populationnelles ont permis de déterminer les valeurs biologiques de base des PBDE chez les travailleurs des populations générales canadienne et états-unienne, et d'identifier les secteurs industriels les plus exposés. Ensuite, une revue systématique de littérature a recensé les niveaux d'exposition professionnelle aux ignifuges dans diverses industries en portant un regard critique sur les méthodes de prélèvement. Finalement, des prélèvements d'air en poste personnel, d'urine et de sang ont été réalisés auprès de 100 travailleurs dans six entreprises de recyclage électronique et une de recyclage commercial. Des modèles Tobit et des régressions de Cox inversées ont identifié les tâches les plus exposantes. L'association entre les mesures biologiques d'exposition et les niveaux d'hormones thyroïdiennes et sexuelles a été explorée avec des modèles Tobit et des régressions sur composantes principales.

L'analyse des données populationnelles a révélé que les travailleurs canadiens, tous secteurs confondus, avaient des concentrations sériques de PBDE 10 à 20% plus élevées que celles des non-travailleurs. La revue systématique a identifié les milieux du recyclage électronique, de la fabrication de câbles, du transport aérien et des casernes d'incendie comme étant parmi les plus exposants aux ignifuges, particulièrement au BDE209. Cependant, les méthodes de prélèvement utilisées dans ces études étaient généralement peu appropriées pour les ignifuges. L'analyse des données de l'étude terrain a mis en évidence des concentrations d'ignifuges dans l'air plus élevées dans le recyclage électronique que dans le recyclage commercial, avec une concentration en BDE209 plus élevée que toutes les valeurs publiées à ce jour (moyenne géométrique [MG] : 5100 ng/m^3). Les tâches de démantèlement et de compactage étaient

respectivement associées à des expositions en moyenne 2,2 et 1,4 fois plus élevées que celle de supervision. Finalement, les concentrations sanguines de BDE209 (MG : 18 ng/g lipides) chez les travailleurs du recyclage électronique étaient plus élevées que dans le recyclage commercial (MG : 1,7 ng/g lipides), mais moins élevées que celles rapportées dans la fabrication de câbles (moyenne : 54 ng/g lipides). On a estimé chez l'homme des diminutions de 18% de la testostérone libre et totale pour un doublement de la concentration de tb-TPhP (métabolite OPE), et une augmentation de 16% de l'estradiol pour un doublement de la concentration de o-iPr-DPhP (métabolite OPE).

Cette thèse montre que l'exposition aux ignifuges est très répandue, particulièrement chez les travailleurs de quelques industries. Les concentrations plus élevées de certains ignifuges dans le recyclage électronique par rapport aux autres industries, et l'association entre l'exposition aux OPE et les niveaux d'hormones sexuelles chez l'homme ont été identifiées pour la première fois. Bien que devant être reproduits, ces résultats justifient des efforts préventifs de maîtrise de l'exposition aux ignifuges dans cette industrie.

Mots-clés :

Ignifuges, polybromodiphényléthers, esters d'organophosphoré, exposition professionnelle, recyclage électronique, ECMS, NHANES, évaluation de l'exposition, modèles Tobit, analyse en composantes principales.

Abstract

Flame retardants are added to various products to comply to flammability standards. The most common are polybrominated diphenyl ethers (PBDEs) and organophosphate esters (OPEs), which are detected in high proportion in the general population. A few industries, such as electronic recycling, can expose workers to high levels of flame retardants, some of which are suspected of being endocrine disruptors. The objective of this thesis was to evaluate the exposure to flame retardants in workers and to study the associated endocrine effects.

Three types of data were used. First, two population databases were used to determine baseline PBDE levels for workers in the general population in Canada and the United States, and to identify the major industrial sectors that are exposed the most. Then, a systematic literature review identified levels of occupational exposure to flame retardants in various industries while critically examining sampling methods. Finally, personal air, urine and blood samples were collected from 100 workers in six electronic recycling and one commercial recycling companies. Tobit models and reverse Cox regressions identified the most exposing tasks. The association between biological concentrations of flame retardants and thyroid and sex hormone levels was explored with Tobit models and principal component regressions.

The analysis of the population data revealed that Canadian workers, taking all sectors into consideration, had serum PBDE levels 10 to 20% higher than those of non-workers. The systematic review identified electronic recycling, cable manufacturing, air transport and fire stations as some of the workplaces where flame retardants were found in the highest concentrations, particularly BDE209. However, the sampling methods used in these studies were generally not optimal for flame retardants. Analysis of the field study data revealed higher air concentrations of flame retardants in electronic recycling than in commercial recycling, with a higher BDE209 concentration than all values published to date (geometric mean [MG]: 5100 ng/m^3). Dismantling and bailing tasks were associated with exposures averaging 2.2 and 1.4 times higher than supervisory tasks, respectively. Finally, blood concentrations of BDE209 (MG: 18 ng/g lipid) in electronic recycling workers were higher than in commercial recycling (MG: 1.7 ng/g lipid), but lower than those reported in cable manufacturing (average: 54 ng/g lipid). Decreases of 18% in free and total testosterone were

estimated in humans for a doubling of the concentration of tb-TPhP (OPE metabolite), and a 16% increase in estradiol for a doubling of the concentration of o-iPr-DPhP (OPE metabolite).

This thesis shows that exposure to flame retardants is widespread, particularly among workers in a few industries. The higher concentrations of some flame retardants in electronic recycling compared with other industries, and the association between exposure to OPEs and sex hormone levels in humans were identified for the first time. Although these results must be reproduced, they justify preventive efforts to control exposure to flame retardants in this industry.

Keywords : Flame Retardants, Polybrominated Diphenyl Ethers, Organophosphate Esters, Occupational Exposure, Electronic Recycling, CHMS, NHANES, Exposure Assessment, Tobit model, Principal Component Analysis.

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Liste des sigles et des abréviations

A
ACGIH : American Conference of Governmental Industrial Hygienists
ACP : Analyse en composantes principales

B
BDE : Congénère de polybromodiphényl éther
BDE100 : 2,2',4,4',6-Pentabromodiphenyl ether
BDE153 : 2,2',4,4',5,5'-Hexabromodiphenyl ether
BDE47 : 2,2',4,4'-Tetrabromodiphenyl ether
BDE99 : 2,2',4,4',5-pentabromodiphenyl ether
BMI : Body mass index

C
CHMS : Canadian Health Measures Survey
ClFR : Ignifuges polychlorés
CTQ : Centre de toxicologie du Québec

D
D3E : Déchets d'équipements électriques et électroniques

E
ECMS : Enquête canadienne sur les mesures de la santé

F
FSH : Hormone folliculostimulante

G
GM : Geometric mean

I
IRSST : Institut de recherche Robert-Sauvé en santé et en sécurité du travail

L
LH : Hormone lutéinisante
LOD : Limit of detection, limite de détection
LOQ : Limit of quantification, limite de quantification

N
NBFR : Nouveaux ignifuges bromés
NHANES : National Health and Nutrition Examination Survey

O
OELs : Occupational exposure limit values

OPE : Esters d’organophosphorés
OPFR : Ignifuges organophosphorés Organophosphate flame retardants
OVS : Occupational Safety and Health Administration (OSHA) Versatile Sampler

P
PBDE : polybromodiphényléthers
PBDEs : Polybrominated diphenyl ethers
PBT : Pentabromotoluène
PRISMA : Preferred Reporting Items for Systematic reviews and Meta-Analyses

Q
QICSS : Quebec inter-University Centre for Social Statistics

R
RCP : Régression sur les composantes principales,
RRPC : Régression à risques proportionnels de Cox

S
SST : Santé et de sécurité au travail

T
T3 : Hormone triiodothyronine
T4 : Hormone thyroxine
TBBPA : Tétrabromobisphénol A
TBOEP : tris-(2-butoxyéthyl) phosphate
TCEP : tris-(2-chloroéthyl) phosphate
TCP : tricrésylphosphate
TCPP : tris(2-chloroisopropyl) phosphate
TPhP : Triphényl phosphate
TSH : Hormone thyréostimuline

À Margot.

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Chapitre 1. Introduction et état des connaissances

1.1. Mise en contexte

La plupart des objets de consommation, appareils électroniques, meubles ou matériaux sont soumis à des normes d'inflammabilité. Ces normes visent à éviter la combustion ou à ralentir la propagation des flammes en cas d'incendie. L'ajout de substances ignifuges à de nombreux produits permet de les conformer à ces normes, et même de dépasser les exigences (Jinhui et al. 2017). Cependant, l'omniprésence des ignifuges est reflétée dans l'environnement, de même que dans les fluides biologiques de la population. Par exemple des ignifuges polybromés peuvent être détectés dans le sang de la population générale, et ce, un peu partout dans le monde (Brasseur et al. 2014; Fromme et al. 2015; Kim et al. 2012).

Depuis les dernières deux décennies, les ignifuges retiennent de plus en plus l'intérêt des chercheurs et décideurs, car on leur a découvert une toxicité chez les organismes vivants. Différentes études ont identifié notamment des effets neurotoxiques et reprotoxiques chez l'humain, mais on leur reconnaît principalement des effets de perturbation du système endocrinien (Hoffman et al. 2018; Kim et al. 2014). Les ignifuges polybromés et organophosphorés ont effectivement été associés à des perturbations des hormones thyroïdiennes et sexuelles chez des modèles animaux et chez des humains.

Les ignifuges sont ubiquitaires dans les maisons, mais certains milieux de travail peuvent exposer les travailleurs à des concentrations plus élevées. C'est le cas du milieu du recyclage électronique. Puisque les appareils électriques et électroniques contiennent beaucoup d'ignifuges (Chen et al. 2012b) qui peuvent être relâchés dans l'air lors des opérations de recyclage, les travailleurs de cette industrie sont susceptibles d'y être plus exposés que la population générale, ou que les travailleurs d'autres industries. Comme la production de déchets électroniques est en constante augmentation dans le monde, ce type d'industrie connaît également une croissance et le nombre de travailleurs exposés à ces substances ne cesse d'augmenter (Premalatha et al. 2014).

Ce projet doctoral a pour but d'augmenter les connaissances sur l'exposition aux ignifuges chez les travailleurs, et plus spécifiquement dans l'industrie du recyclage électronique. De plus, ce projet vise à explorer les associations entre les expositions aux ignifuges et des hormones thyroïdiennes et sexuelles chez les travailleurs du recyclage électronique. Ce projet est associé à une étude financée par l'Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), intitulée :

Évaluation de l'exposition aux contaminants chimiques des travailleurs œuvrant dans le recyclage primaire des matières résiduelles électroniques au Québec et appréciation du risque sanitaire. Projet 2015-0083, chercheurs principaux Joseph Zayed et France Labrèche.

Ce chapitre fait tout d'abord la description des substances ignifuges, en détaillant leurs usages et leur historique, puis l'exposition à ceux-ci dans la population générale et chez les travailleurs du recyclage électronique. La toxicocinétique et la toxicodynamique des substances mesurées dans le cadre de cette thèse sont également abordées. Par la suite, le secteur du recyclage électronique est décrit et les particularités de ce milieu sont présentées. Le chapitre contient enfin un résumé des enjeux, présente les objectifs du projet doctoral et détaille enfin le travail de l'étudiante.

1.2. Les ignifuges

Les ignifuges sont des mélanges de substances chimiques ajoutés aux matériaux durant la fabrication de divers objets afin de réduire le risque que le produit fini ne prenne feu, et de ralentir, le cas échéant, sa combustion. Depuis la deuxième moitié du 20$^{\text{ième}}$ siècle, des ignifuges organiques ont été ajoutés aux tissus, tapis, matelas, équipements électriques et électroniques, meubles, et autres appareils ou objets étant soumis à des normes d'inflammabilité (Dishaw et al. 2014).

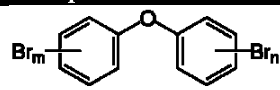
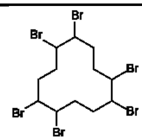
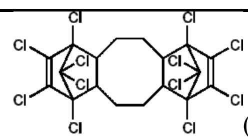
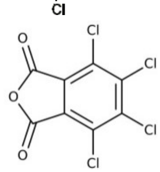
1.2.1. Description

Parmi les ignifuges organiques, on reconnaît quatre grands groupes chimiques (Tableau 1.1). Les plus utilisés et les plus anciens sont les polybromodiphényléthers (PBDE), des molécules constituées de deux cycles aromatiques halogénés comprenant de un à dix atomes de brome. Les mélanges commerciaux de PBDE incluent le pentaBDE, constitué de plusieurs congénères ayant de quatre à six atomes de brome, le octaBDE dans lequel les congénères ont de six à 10 atomes de brome, et finalement le mélange décaBDE qui contient presque exclusivement un congénère à 10 atomes de brome. Puisque des effets néfastes sur les fœtus ont été observés en association avec certains PBDE (Wargo et al. 2013), des ignifuges de substitution ont été mis sur le marché. Notons les nouveaux ignifuges bromés (NBFR), qui sont souvent chimiquement moins persistants lorsqu'ils sont de nature cycloaliphatique (comprenant un cycle de 5 atomes de carbone ou moins) ou aliphatique (ne comprenant aucun cycle de carbone) (Ali et al. 2011; Covaci et al. 2011). Les esters d'organophosphorés (OPE) sont quant à eux généralement utilisés comme plastifiants, mais également employés comme ignifuges de substitution aux PBDE. Ces molécules aliphatiques se déclinent en des dizaines de substances différentes ayant toutes un cœur phosphate lié à quatre atomes d'oxygène, les rendant assez instables et peu persistantes (van der Veen and de Boer 2012). Finalement, des ignifuges polychlorés (ClFR) sont également utilisés, lesquels seraient persistants selon leur structure chimique, mais très peu de données toxicologiques existent à leur sujet (Wang et al. 2016). La plupart des ignifuges ne sont pas liés chimiquement aux matériaux auxquels ils sont ajoutés (Webster and Stapleton 2012). Étant principalement des composés organiques semi-volatils, ils peuvent se volatiliser et s'adsorber aux poussières et particules en suspension, ou encore se disperser avec les débris de matières friables comme le plastique et la fibre de verre (Takigami et al. 2008; Webster et al. 2009; Webster and Stapleton 2012).

Ignifuges dans les équipements électroniques

Les ignifuges entrent dans la composition de plusieurs matériaux, mais on les retrouve généralement en forte concentration dans les appareils électroniques. Certaines substances ont été plus utilisées : c'est le cas du congénère BDE209, très fréquent dans les appareils électroniques, et principalement dans les téléviseurs à tubes cathodiques (Aldrian et al. 2015). On peut le retrouver dans presque tous leurs composants, depuis les cartes de circuits imprimés jusqu'aux boîtiers en polymères, en passant par les gaines de fils électriques (Jinhui et al. 2017). Plus récemment, de nouveaux ignifuges sont utilisés en remplacement des PBDE et comprennent notamment le 1,2,3,4,7,8,9,10,13,13,14,14-dodécachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodécahydro-1,4,7,10-dimethanodibenzo[a,e]cyclooctene (Déchlorane Plus), un ignifuge polychloré (ClFR), ainsi que différents OPE comme le triphényle phosphate (TPhP) ou le tris(2-chloroéthyle) phosphate (TCEP) et des NBFR comme le tétrabromobisphénol A (TBBPA) et l'hexabromobenzène (HBB) (Deng et al. 2014; Dishaw et al. 2014; Julander et al. 2005b; Stapleton et al. 2011; Vonderheide et al. 2008). Ces substances sont également retrouvées dans toutes les composantes des appareils électroniques (Vonderheide et al. 2008).

Tableau 1.1. Groupes chimiques d'ignifuges et propriétés physico-chimiques

Groupe chimique	**Structure générale ou exemple**	**Usages communs**	**Statut réglementaire au Canada**	**Pression de vapeur (Pa)**	**Log K_{ow}**
Polybromodiphényléthers (PBDE)		• Boîtiers d'appareils électroniques • Cartes de circuits imprimés • Mousse de polyuréthane	• PentaBDE et octaBDE : interdiction de production et d'usages nouveaux en 2008 • DecaBDE : retrait volontaire par les 3 fabricants canadiens en 2010	De $5{,}7\times10^{-7}$ à 0,16	De 5,9 à 10
Nouveaux ignifuges bromés (NBFR)	 (HBCD)  (PBT)	• Adhésifs • Textiles enduits • Gaines de fils électriques	• Aucun NBFR n'est réglementé • Certains n'ont pas été évalués quant à leur toxicité • Certains font partie du « Plan de gestion des produits chimiques »	De $2{,}0\times10^{-25}$ à 0,41	De 3,3 à 13
Esters d'organophosphorés (OPE)	[redacted]	• Textiles • Mousse de polyuréthane • Revêtements de PVC	• Le triphényle phosphate est réglementé pour la santé au travail • Certains n'ont pas été évalués quant à leur toxicité • Certains font partie du « Plan de gestion des produits chimiques »	De $9{,}9\times10^{-6}$ à 39	De 0,8 à 9,5
Ignifuges polychlorés (ClFR)	 (DP)  (TCP-Anh)	• Gaines de fils électriques • Matériaux de construction	• Certains n'ont pas été évalués quant à leur toxicité • Certains font partie du « Plan de gestion des produits chimiques »	De 0,80 à 21	De 4,7 à 9,3

Références : Covaci et al. (2011); Eljarrat and Barceló (2011); Environnement Canada (2013); Wang et al. (2016); Wei et al. (2015)
Abréviations : HBCD – hexacyclobromododécane; PBT – pentabromotoluène; DP – Dechlorane Plus; TCP-Anh – anhydride tétrachlorophtalique

1.2.2. Exposition

Dans la population générale

Puisque les ignifuges sont pratiquement ubiquitaires dans les matériaux et peuvent facilement s'en dégager, la population générale et les travailleurs de diverses industries ont une grande probabilité d'y être exposés. Les poussières dans les maisons peuvent en effet présenter des concentrations relativement élevées. Venier et al. (2016) ont mesuré dans la poussière déposée de maisons ontariennes des médianes de 713 ng/g de BDE209, 6,1 ng/g de HBB et 15 ng/g de *anti*Déchlorane Plus (aDP), de même que des concentrations de 0,049 ng/m³ de BDE209, de 0,0058 ng/m³ de HBB et de 0,025 ng/m³ de aDP dans l'air de ces mêmes maisons. Dans la même province, des concentrations de 0,72 à 2,4 ng/m³ de TPhP et de 3,0 ng/m³ de pentabromotoluène (PBT, un NBFR) ont été mesurées dans l'air d'autres maisons (Okeme et al. 2018; Vykoukalova et al. 2017). Ceci laisse présumer d'une exposition domestique et environnementale non négligeable aux ignifuges de différents groupes chimiques au Canada.

Tableau 1.2. Concentration sérique de congénères de PBDE dans la population générale de différents pays (ng/g lipides)

Pays	Année	Population	Indica-teur[a]	N	Congénères de PBDE (ng/g lipides) BDE209	BDE183	BDE153	BDE99	BDE47	Référence
Allemagne	2013	Adultes	Med	70	--	0,12	0,97	0,16	0,38	Fromme et al. (2015)
Canada	2007-2009	Adultes 20-39 ans	MG	4583	1,4	0,36	11	4,6	21	Rawn et al. (2014)
Corée du Sud	2006	Adultes	Med	103	--	ND	1,8	1,2	2,2	Kim et al. (2018)
Espagne	2002	Adultes	MG	731	3,5	0,27	0,74	1,1	2,2	Gari and Grimalt (2013)
États-Unis	2003-2004	Adultes 20-39 ans	MG	?	--	--	6,6	5,2	22	Sjodin et al. (2008)
États-Unis	2008-2009	Adultes	MG	90	1,3	0,13	6,8	3,4	21	Wu et al. (2015)
États-Unis	2011-2015	Femmes 40-94 ans	Med	1253	--	--	4,9	--	13	Hurley et al. (2017)
France	2003-2005	Adultes	Med	48	--	--	1,39	0,49	2,1	Brasseur et al. (2014)
Nouvelle-Zélande	2001	Adultes	Med	23	--	0,23	1,0	0,80	3,2	Harrad and Porter (2007)

[a] Med, médiane; MG, moyenne géométrique; ND, non décelé; --, non mesuré

Le fait que des concentrations mesurables d'ignifuges soient retrouvées dans le sang de la population générale (Tableau 1.2) témoigne également de leur omniprésence dans l'environnement. En effet, les données provenant de l'Enquête canadienne sur les mesures de santé (ECMS) révèlent que la concentration sanguine moyenne géométrique de BDE47 chez des Canadiens âgés de 20 à 39 ans était de 21 ng/g lipides pour la période 2007-2009 (Rawn et al. 2014). Bien que ces données aient été colligées il y a plus d'une décennie, il s'agit de la plus récente et complète recension des niveaux sériques d'ignifuges dans la population générale canadienne. Il n'existe pas, à ce jour, de données biologiques d'enquêtes pancanadiennes sur l'exposition à des OPE, des ClFR ou des NBFR, quoique quelques études rapportent des concentrations de métabolites urinaires d'OPE (Tableau 1.3).

Tableau 1.3. Concentration urinaire de métabolites d'OPE dans la population générale de différents pays (ng/ml, ajusté sur la gravité spécifique)

					Métabolite d'OPE (ng/ml, ajusté sur gravité spécifique)		
Pays	Années	Population	Indicateur[a]	**N**	DPhP	BDCiPP	**Référence**
Australie	2012-2013	Hommes et femmes 0-75 ans	MG	2300	63	0,66	Van den Eede et al. (2015)
Canada[b]	2015	Femmes	MG	44	12	0,74	Yang et al. (2019)
États-Unis	2013-2014	Femmes adultes	MG	22	1,9	2,4	Butt et al. (2014)
États-Unis[b]	2006	Adultes	Med	16	0,44	0,09	Dodson et al. (2014)
États-Unis	2002-2015	Adultes	MG	741	1,5	1,3	Hoffman et al. (2017a)
États-Unis	2002-2007	Hommes adultes	MG	7	0,31	0,13	Meeker et al. (2013b)

[a] Med, médiane; MG, moyenne géométrique
[b] Résultats non ajustés sur la gravité spécifique
DPhP : Diphényl phosphate; BDCiPP : bis(1,3-dichloro-2-propyl) phosphate

Au Canada, il existe des recommandations fédérales quant à la présence de PBDE dans l'environnement pour protéger la faune, mais il n'y a pas de concentration maximale acceptable établie pour l'eau potable et ce, pour aucun ignifuge. Il n'y a pas non plus de valeurs guide biologiques pour ces substances. En milieu de travail, seul le TPhP fait l'objet d'une valeur limite d'exposition professionnelle dans le Règlement sur la santé et la sécurité du travail québécois (Gouvernement du Québec 2019b), laquelle est fixée à 3 mg/m³ sur la base de données de toxicité neurologique et d'irritation pour la peau et les yeux (American Conference of Governmental Industrial Hygienists 2019).

Expositions professionnelles

Certains milieux de travail peuvent présenter des niveaux d'exposition plus élevés que ceux des milieux résidentiels. Pensons notamment aux tours de bureaux où le mobilier et les électroniques sont abondants (moyenne géométrique [MG] BDE47 dans l'air : 0,26 ng/m^3) (Watkins et al. 2013), aux avions où les exigences réglementaires d'inflammabilité sont sévères (MG BDE47 dans l'air : 1,3 ng/m^3) (Allen et al. 2013b), ou encore au métier de pompier dont les vêtements de protection contiennent des ignifuges provenant du matériau lui-même et d'une contamination externe (médiane BDE47 dans le sang : 25 ng/g lipides) (Shaw et al. 2013).

Dans le recyclage électronique, les opérations de démantèlement et de broyage des appareils peuvent libérer les ignifuges entrant dans leur composition, lesquels peuvent être inhalés par les travailleurs (Kim et al. 2015; Lecler et al. 2015; Tsydenova and Bengtsson 2011). De plus, les poussières retrouvées dans de vieux boîtiers de télévision – lesquelles sont remises en circulation lors de la manipulation et du démantèlement des appareils – peuvent contenir de deux à trois fois la quantité d'ignifuges retrouvée généralement dans les poussières déposées des maisons (Deng et al. 2014; Takigami et al. 2008). Une étude suédoise menée par Sjodin et al. (2001) a rapporté des concentrations de PBDE dans l'air ambiant allant de 150 à 175 ng/m^3 au voisinage d'une déchiqueteuse de résidus électroniques, alors qu'elles étaient seulement de 0,35 ng/m^3 dans une usine d'assemblage de circuits imprimés. D'autres chercheurs suédois ont mesuré des concentrations allant de 158 à 209 ng/m^3 de PBDE totaux dans les poussières ambiantes inhalables, où le congénère BDE209 était le plus présent (2,8 à 3,3 ng/m^3 dans les poussières inhalables) (Julander et al. 2005b). En Finlande, les concentrations de PBDE totaux et de TBBPA se situaient respectivement entre 21 et 2320 ng/m^3 et entre 8,7 et 430 ng/m^3 dans la zone respiratoire des travailleurs du recyclage électronique (Rosenberg et al. 2011). Dans une autre étude finlandaise comparant l'exposition aux OPE dans différents milieux de travail, les moyennes géométriques de TBBPA dans la zone respiratoire des travailleurs dans le recyclage électronique se situaient autour de 1000 ng/m^3, et de 800 ng/m^3 pour le TPhP, ce qui était nettement supérieur aux concentrations dans une usine de fabrication de circuits imprimés, un atelier de meubles et un immeuble de bureaux où ces substances n'avaient été que peu ou pas détectées (Makinen et al. 2009). Finalement, dans cinq établissements d'entreposage de déchets électroniques en Thaïlande, les concentrations mesurées dans l'air étaient beaucoup plus basses, allant de 0,046 à 0,35 ng/m^3 (Muenhor et al. 2010).

Peu d'études ont mesuré l'exposition aux ignifuges par le biais de biomarqueurs chez des travailleurs. Sjodin et al. (1999) ont mis en évidence des concentrations sériques moyennes de PBDE (somme des congénères 47, 153, 154, 183 et 209) de 26 ng/g lipides chez des travailleurs d'une entreprise de démantèlement de D3E. Ces valeurs étaient plus élevées que celles mesurées chez des commis informatiques et chez des préposés au nettoyage en milieu hospitalier qui présentaient respectivement 3,3 et 7,1 ng/g lipides en PBDE totaux. Une étude chez des travailleurs du recyclage électronique informel (entreprises non constituées en sociétés qui ne sont pas enregistrées auprès de l'état, http://uis.unesco.org/fr/glossary-term/secteur-informel) en Chine a pu mesurer une valeur sérique médiane de PBDE (somme de 17 congénères) de 753 ng/g lipides (Zheng et al. 2014). Il faut souligner que la mesure de l'exposition en termes de somme massique de congénères, utilisée dans différentes études, présente des limites. En effet, les congénères inclus dans la somme varient d'une étude à l'autre, et l'unité massique plutôt que molaire rend compte moins précisément de l'importance toxicologique relative de chaque congénère.

Il n'existe aucune valeur limite d'exposition en milieu de travail pour les ignifuges bromés ou chlorés au Canada, ou dans d'autres pays. En ce qui a trait aux OPE, seul le TPhP présente une valeur limite d'exposition professionnelle de 3 mg/m^3 (American Conference of Governmental Industrial Hygienists 2019). Cette concentration a été établie pour prévenir des effets neurotoxiques ainsi que l'irritation de la peau et des yeux. On soupçonne toutefois que l'exposition aux ignifuges chez les travailleurs pourrait être associée à un dérèglement de l'équilibre hormonal, lequel pourrait éventuellement occasionner pour les travailleurs divers problèmes de santé aux niveaux digestif, cardiaque et reproducteur (Czerska et al. 2013; De Coster and van Larebeke 2012; Grant et al. 2013). De plus, les expositions à des mélanges complexes de diverses substances peuvent avoir des effets qui sont encore méconnus (Gore et al. 2015).

1.2.3. Toxicocinétique

Plusieurs auteurs supposent que l'ingestion par inadvertance de poussières est la voie d'absorption principale aux ignifuges dans la population générale, suivie, dans une moindre mesure, par la consommation d'aliments contaminés, par l'inhalation, puis par pénétration cutanée (Abou-Elwafa Abdallah et al. 2016; Allen et al. 2008; Frederiksen et al. 2009; Watkins et al. 2012). En milieu de travail, l'absorption des ignifuges se fait probablement de façon majoritaire par inhalation, mais une certaine proportion peut également pénétrer la peau ou être ingérée par inadvertance. À des fins de calcul des doses absorbées, les auteurs estiment une ingestion journalière moyenne de poussières domestique chez les adultes de 20 mg/jour et de 50 mg/jour pour des travailleurs (Hearn et al. 2013; Roosens et al. 2009). Toutefois, les études de corrélations entre les différents médias (poussières, aliments et sang, par exemple) peinent à démontrer quelles voies d'absorption sont effectivement majoritaires (Bramwell et al. 2017). De manière expérimentale, il a été démontré que les PBDE peuvent présenter chez l'humain une absorption cutanée de tout au plus 30% de la dose d'exposition pour les congénères ne comprenant qu'un seul atome de brome. Plus la bromation augmente, moins les PBDE pénètrent la peau (Abdallah et al. 2015). Quant aux OPE, le pourcentage d'absorption cutanée se situerait entre 9% et 28%, selon la substance et la méthode expérimentale employée (Abou-Elwafa Abdallah et al. 2016; Hughes et al. 2001). Les NBFR et ClFR testés ont une absorption cutanée chez l'humain un peu inférieure, soit de 8% à 13% (Frederiksen et al. 2016).

Il n'y a pas d'études rigoureuses sur la distribution de substances ignifuges chez l'humain. Nous savons cependant que la distribution des PBDE dans les lipides diminue à mesure que le nombre d'atomes de brome augmente, en dépit d'un coefficient de partition éthanol-eau (K_{ow}) qui augmente avec le nombre d'atomes de brome (U.S. Environmental Protection Agency 2008a; b). Cela s'explique possiblement par une masse moléculaire et une conformation qui inhibe leur pénétration dans les adipocytes, à mesure que le nombre d'atomes de brome augmente.

Le métabolisme de la plupart des ignifuges n'est pas encore totalement élucidé et les informations les plus complètes sont obtenues à partir de modèles animaux. Les PBDE ne sont que très peu métabolisés, et il est estimé que tout au plus 1% des PBDE absorbés est hydroxylé et méthoxylé, produisant des métabolites plus toxiques que la substance mère (Dingemans et al. 2011; Ren et al. 2013; Wiseman et al. 2011). On rapporte aussi une débromation des PBDE, sans connaître avec précision la proportion qui sera métabolisée de cette manière (Thuresson et al. 2006b). Par conséquent, l'indicateur biologique le plus approprié pour les PBDE consiste en la substance mère dans le sang (sérum ou plasma, selon la méthode d'analyse). Les concentrations sanguines des différents congénères de PBDE seront généralement ajustées sur les lipides sanguins totaux ou en fonction du poids humide sérique, afin de refléter la charge corporelle de manière plus appropriée. Les OPE, à l'instar des pesticides organophosphorés, sont généralement rapidement métabolisés et plusieurs de leurs métabolites sont mesurables dans l'urine, dont certains sont spécifiques à la substance mère et d'autres non (Hou et al. 2016; Van den Eede et al. 2013). Par exemple, on a identifié quatre métabolites potentiels du tris(1-chloro-2-propyl) phosphate (TDCiPP), dont seulement deux ont vu leur structure moléculaire confirmée (Van den Eede et al. 2016). Ces métabolites sont généralement ajustés sur la gravité spécifique de l'urine, afin d'unifier les mesures dans une population, sans égard pour l'hydratation, l'excrétion urinaire, l'âge ou encore le sexe (MacPherson et al. 2018).

Les demi-vies biologiques des ignifuges ne sont pas toutes connues chez l'humain. Certains congénères de PBDE, comme le BDE153, sont très lipophiles et contribuent à une charge corporelle élevée et ont une demi-vie apparente de plus de 6 ans (Geyer et al. 2004; Harju et al. 2009; Patisaul et al. 2013). Généralement, plus le nombre d'atomes de brome augmente, plus la demi-vie des congénères de PBDE est courte, jusqu'au décaBDE dont la demi-vie se situe autour de 15 jours (Thuresson et al. 2006b). Les OPE sont généralement plus hydrophiles que les PBDE et leur demi-vie est beaucoup plus courte, soit de l'ordre de quelques heures (Hou et al. 2016; Meeker et al. 2013b).

1.2.4. Toxicodynamique

Des effets physiologiques chez l'humain ont été observés en association avec une exposition aux ignifuges, comme une neurotoxicité et des troubles du développement chez l'enfant, une reprotoxicité, et principalement, des désordres hormonaux. Les PBDE, tout comme les OPE, ont été associés à des effets délétères chez l'enfant à la suite d'une exposition prénatale. Les données sont plus solides et étoffées dans les modèles cellulaires et les modèles animaux que chez l'humain (Hendriks and Westerink 2015), mais quelques études ont montré des associations entre les ignifuges et des problèmes neurologiques ou reproducteurs. Par exemple, on a mesuré une motricité fine moindre et des troubles de l'attention chez des enfants dont les mères avaient au moment de la grossesse des concentrations sériques de PBDE totaux au-delà de 42 ng/g de lipides (Eskenazi et al. 2013). On a également noté une augmentation du risque d'accouchement prématuré chez des mères ayant des concentrations urinaires de Bis (1,3-dichloro-2-propyl) phosphate (BDCiPP, un métabolite du TDCiPP) au-delà de 0.42 ng/ml (Hoffman et al. 2018). Les effets associés à une exposition aux ignifuges les plus rapportés demeurent les désordres hormonaux, ou perturbations endocriniennes (Gore et al. 2015; Lyche et al. 2015). Une exposition à ces substances peut en effet être associée à des variations des concentrations d'hormones thyroïdiennes ou sexuelles circulantes. Les manifestations cliniques d'un déséquilibre thyroïdien peuvent inclure la fatigue, une perte ou un gain de poids, des palpitations cardiaques ou encore d'autres dérèglements homéostatiques (Koulouri et al. 2013). Les effets sur les hormones sexuelles peuvent quant à eux se manifester principalement par une altération d'indicateurs de fertilité, comme la qualité du sperme ou le délai de conception, entre autres (Balabanic et al. 2011). La section suivante décrit plus en détail l'étendue des connaissances sur les associations entre l'exposition à des ignifuges et les niveaux d'hormones.

Perturbation endocrinienne

La perturbation des niveaux d'hormones par des xénobiotiques est de plus en plus étudiée, dans un contexte où la définition d'un « perturbateur endocrinien » ne fait cependant pas encore l'unanimité (Gore et al. 2015; Henrotin 2013). En effet, l'Organisation mondiale de la santé (OMS) les définit comme étant des substances ou mélanges de substances qui altèrent des fonctions du système endocrinien, ce qui par conséquent augmente la probabilité de survenue d'effets nocifs sur la santé. L'OMS distingue les « perturbateurs endocriniens potentiels » comme étant des substances qui ont des propriétés desquelles on pourrait s'attendre à ce qu'elles occasionnent une perturbation endocrinienne (World Health

Organization 2013). La Endocrine Society, composée de groupes de chercheurs et de médecins, fait plutôt référence à des substances chimiques exogènes qui interfèrent avec tout aspect de l'action des hormones (Gore et al. 2015). La nuance est importante, parce que le premier sous-entend que la perturbation endocrinienne est un mécanisme menant éventuellement à la toxicité, tandis que l'autre sous-entend que la perturbation de cet état d'équilibre est un effet nocif en soi. Tous sont cependant d'avis que les mécanismes de toxicité des perturbateurs endocriniens sont d'importance tant pour la santé humaine et la reproduction, que pour l'environnement. Dans cette thèse, la position de la Endocrine Society est favorisée, dans la perspective où l'étude des effets endocriniens en amont d'effets nocifs à la santé constitue une avenue intéressante pour la prévention en matière de santé au travail.

Le système endocrinien régit un équilibre crucial entre les différentes hormones nécessaires au bon fonctionnement de l'organisme. Cette homéostasie peut être perturbée de manière endogène, ou par des substances toxiques qui agissent à différents niveaux, soit sur les récepteurs hormonaux, sur la synthèse des hormones et des intermédiaires, ou sur la réponse physiologique (De Coster and van Larebeke 2012; Diamanti-Kandarakis et al. 2009). Il est généralement considéré que les courbes dose-réponse pour la perturbation endocrinienne ne sont pas classiques, c'est-à-dire présentant une dose seuil sécuritaire. En effet, un perturbateur endocrinien peut occasionner à faible dose des effets biologiques différents ou plus importants que ceux observés à plus forte dose (Vandenberg et al. 2012; Zhu et al. 2014). On a également observé des courbes dose-réponse non monotones, c'est-à-dire des courbes où la pente change de signe à mesure que la dose augmente (Figure 1.1) (Beausoleil et al. 2016). Les effets endocriniens des PBDE sont de mieux en mieux compris, mais les études sont encore peu concluantes pour les OPE (Fonnum et al. 2006; Lyche et al. 2015; Meeker and Stapleton 2010). Parmi les nombreux perturbateurs endocriniens potentiels ou avérés, les ignifuges sont de plus en plus l'objet d'études de toxicité au niveau de l'équilibre hormonal, dans des modèles cellulaires, animaux, et chez l'humain.

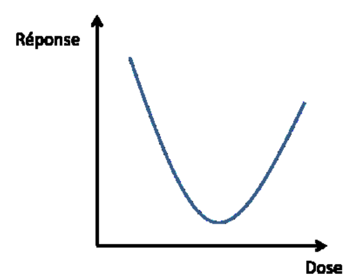


Figure 1.1. Courbe dose-réponse non-monotone

Dans les études *in vitro* et *in vivo*

Les ignifuges bromés ont fait l'objet d'essais de toxicité en laboratoire, tant *in vitro* qu'*in vivo* dans une variété d'espèces animales (Darnerud 2008; Dorosh et al. 2011). Par mimétisme, les métabolites hydroxylés de PBDE et les substances mères peuvent se lier de manière compétitive aux transporteurs sériques des hormones thyroïdiennes, aux enzymes métaboliques, ainsi qu'aux récepteurs thyroïdiens. Cette imitation complète ou partielle (figure 1.1) de l'hormone offre alors aux PBDE plusieurs mécanismes par lesquels ils pourraient agir sur la régulation thyroïdienne (Dishaw et al. 2014). Chez les poissons et différents rongeurs, certains congénères de PBDE sont associés à un effet inhibiteur sur la thyroxine (T4), alors qu'il y a plus d'ambiguïté au sujet des hormones triiodothyronine (T3) et thyréostimuline (TSH) (Chen et al. 2012a; Czerska et al. 2013; Yu et al. 2010). Toujours dans des études *in vivo* chez des rongeurs, une diminution des hormones estradiol (E2) et testostérone a été observée, de même qu'une puberté retardée associée spécifiquement au BDE99 (Lilienthal et al. 2006). Les résultats de ces études sont cependant très hétérogènes, selon l'espèce animale, la dose, ou le congénère étudié. Une équipe de l'Université McGill à Montréal a exposé des rats à un mélange de congénères de PBDE représentatif des poussières domestiques. Une toxicité hépatique a été observée, mais pas de changements significatifs au niveau des hormones thyroïdiennes ou reproductrices (Ernest et al. 2012).

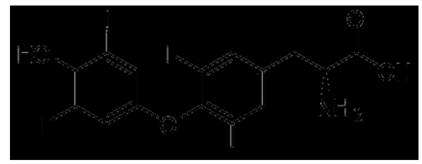


Figure 1.2. Structure moléculaire de l'hormone thyroxine (T4)

Des études toxicologiques ont montré que les OPE pourraient avoir des effets néfastes sur le système endocrinien et la reproduction chez l'animal à la suite d'une exposition à long terme, mais leur mécanisme d'action n'est pas encore élucidé (Dishaw et al. 2014; Hou et al. 2016). Dans un essai *in vitro* avec des OPE, les substances TCEP, tris-(1,3-dichloro-2-propyl) phosphate (TDCiPP), tris-(2-butoxyéthyl) phosphate (TBOEP), TPhP, et tricrésylphosphate (TCP) ont augmenté considérablement la production de testostérone par des cellules adrénocorticales humaines. De même, le TCP, TDCiPP, et TPhP ont été associés à une augmentation de la concentration sérique de testostérone chez le poisson-zèbre mâle (Liu et al. 2012).

Chez l'humain adulte

Chez l'humain, les effets de l'exposition à des ignifuges sur les niveaux hormonaux et sur la santé ont été étudiés particulièrement chez le fœtus en développement et chez les enfants (Kim et al. 2014; Linares et al. 2015), et plus rarement chez les adultes (Zhao et al. 2015). Cependant, il y a peu d'études sur les effets des OPE, des NBFR ou des ClFR, comparativement aux études portant sur les PBDE. De plus, les différentes études rapportent parfois des effets contradictoires.

Chez l'homme, certains congénères de PBDE ont été associés aux niveaux d'hormones circulantes, ou encore à des effets physiologiques. Le BDE153 sérique de jeunes Japonais (moyenne géométrique : 0,69 ng/g lipides) a été associé à une diminution du nombre de spermatozoïdes, tout en demeurant au-delà des minimums requis pour la fertilité (Akutsu et al. 2008). Chez 24 hommes recrutés dans une clinique de fertilité, les congénères BDE47, 99 et 100 présents dans la poussière de leur maison étaient associés à une concentration plus faible des hormones folliculostimulante (FSH) et lutéinisante (LH), et à une augmentation de T4 libre (Meeker et al. 2009). Une équipe américaine a également étudié l'association entre les niveaux d'hormones et la teneur en ignifuges bromés dans la poussière domestique chez 38 hommes. Le mélange octaBDE était directement associé aux concentrations des hormones T4, TSH, LH et testostérone, alors que le décaBDE était inversement associé à la testostérone seulement (Johnson et al. 2013). Quelques études ont été effectuées chez des groupes de femmes enceintes (Chevrier et al. 2010; Gao et al. 2016; Kim et al. 2013; Stapleton et al. 2011). Les associations entre les concentrations en PBDE et les hormones thyroïdiennes ou sexuelles ne concordent pas d'une étude à l'autre, mais on peut penser que les résultats hormonaux durant la grossesse sont difficilement extrapolables aux femmes non enceintes (Fisher 1996).

Certains congénères de PBDE ont été associés à des modifications des concentrations hormonales chez des groupes de travailleurs plus exposés que la population générale. Par exemple, une étude américaine chez 52 travailleurs de bureau masculins a estimé qu'une augmentation sérique de 1 ng/g des congénères BDE47 et BDE100 entraînait une diminution de 2,6 µg/dL et 7,8 µg/dL de T4, respectivement (Makey et al. 2016a).

Les données sur les effets des OPE chez l'adulte sont plus rares que celles sur les PBDE. Une étude a montré qu'une exposition au TDCiPP dans les poussières pouvait être associée à une diminution de T4 et une augmentation de l'hormone prolactine, ainsi qu'à une diminution de la qualité du sperme chez l'homme (Meeker and Stapleton 2010). Plusieurs issues de grossesse chez des femmes suivies en fertilisation *in vitro* ont été associées aux niveaux urinaires de métabolites d'OPE, comme une diminution de 10% du succès de la fertilisation, une diminution de 31% du succès d'implantation, et une diminution des grossesses de 41% (Carignan et al. 2017).

En général, les études épidémiologiques sur les effets d'une exposition aux ignifuges présentent des lacunes expérimentales, entre autres des mesures de l'exposition imprécises et des tailles d'échantillon relativement faibles. Par exemple, citons Johnson et al. (2013) qui ont rapporté une association entre la teneur en PBDE de la poussière déposée dans les maisons et certaines hormones : l'utilisation de la concentration en ignifuges dans les poussières déposées comme indicateur de l'exposition sous-entend une ingestion et une pénétration cutanée considérables des ignifuges, en plus de l'inhalation. Bien que cela soit mentionné par plusieurs auteurs, il ne semble pas y avoir de données solides qui démontrent laquelle de ces voies d'exposition est effectivement majoritaire. De plus, la mesure des effets se fait surtout par le dosage des hormones libres ou totales, alors que la mesure des ratios d'hormones pourrait révéler plus d'informations sur les mécanismes de toxicité sous-jacents (Koulouri et al. 2013; Lien et al. 2017). En effet, le ratio d'une hormone libre sur son équivalent total (libre + conjugué aux protéines de transport) peut mettre en évidence des effets sous-cliniques témoignant de l'adaptation de l'organisme à la présence de xénobiotiques (Sollberger and Ehlert 2016).

Effets observés chez les travailleurs du recyclage électronique

Quelques études ont porté plus spécifiquement sur les effets d'une exposition aux ignifuges dans le contexte du recyclage électronique formel (Grant et al. 2013). En Suède, les hormones thyroïdiennes et l'exposition aux PBDE de 11 travailleuses du recyclage électronique ont été mesurées à quelques reprises pendant un an et demi. Les chercheurs n'ont cependant pas pu mettre en évidence des différences significatives entre les niveaux hormonaux des travailleuses peu exposées et les plus exposées (médiane de BDE47 de 1,4 à 2,8 ng/g lipides)

(Julander et al. 2005a). Une autre étude chez 111 travailleurs du recyclage électronique au Vietnam (médiane BDE47 et BDE209 chez le groupe témoin : 0,12 ng/g lipides et non détecté ; et chez les exposés : 0,16 et 0,023 ng/g lipides) n'a pas mis en évidence d'association entre les hormones thyroïdiennes et l'exposition aux PBDE (Eguchi et al. 2015). Deux études chinoises ont rapporté que des personnes ayant travaillé au démantèlement de résidus électroniques avaient un niveau sanguin d'hormone TSH significativement différent des niveaux d'un groupe témoin, mais l'une a mesuré un niveau plus élevé et l'autre plus bas, comparativement au groupe témoin (Wang et al. 2010; Yuan et al. 2008). Dans l'étude de Wang et al. (2010), le groupe exposé avait une concentration médiane de BDE209 de 41 ng/g lipides, et le groupe témoin de 28 ng/g lipides. Quant aux sujets de l'étude de Yuan et al. (2008), la somme médiane des congénères de PBDE s'élevait à 382 ng/g de lipides pour le groupe exposé et à 158 ng/g lipides pour les non-exposés.

1.3. Le recyclage électronique

L'augmentation de la consommation domestique, de même que l'obsolescence subjective ou fonctionnelle du matériel technologique ont contribué au cours des dernières décennies à l'augmentation substantielle de la production de déchets d'équipements électriques et électroniques (D3E), et conséquemment, à l'augmentation du recyclage de ceux-ci (Baldé et al. 2015; Premalatha et al. 2014; Zhang et al. 2012). Les déchets d'équipements électriques et électroniques (D3E) incluent notamment des ordinateurs et des écrans, des imprimantes et des télécopieurs, des téléviseurs, des téléphones, ainsi que d'autres petits appareils électroniques (Recyc-Québec 2009).

1.3.1. L'industrie du recyclage électronique au Québec

Il y a au Québec une cinquantaine d'entreprises de recyclage électronique primaire, employant plus de 500 travailleurs et il est attendu que ce nombre augmente au cours des prochaines années. Le recyclage électronique primaire consiste généralement dans le tri et le démantèlement manuel ou mécanisé des appareils. Au Québec, il y a quelques entreprises privées gérant un grand volume de matériel électronique, mais la majorité est constituée de plus petites entreprises. Ces dernières sont soit des entreprises privées employant une dizaine de travailleurs, ou encore des entreprises à but non lucratif et ayant une vocation sociale. On distingue également le recyclage électronique formel du recyclage électronique informel. Le recyclage formel des D3E fait référence aux activités menées dans des installations autorisées ou sous le contrôle d'une autorité légale et qui sont conformes aux lois et réglementations environnementales (McCann and Wittmann 2015). En revanche, le recyclage informel est considéré comme peu réglementé, potentiellement plus dommageable, et se déroule généralement dans des ateliers de petite taille et dispersés ou dans des lieux domestiques. Il n'est pas exclu que des opérations de recyclage informel aient lieu au Québec, car n'importe qui peut mettre la main sur de vieux appareils électroniques et en retirer les composants de valeur. De même, malgré que beaucoup de recherches portent sur le recyclage informel dans des pays comme la Chine, le Ghana ou l'Inde, il s'y trouve également des d'entreprises de recyclage électronique formel (Deng et al. 2014; Eguchi et al. 2015).

1.3.2. Description du milieu de travail et des tâches

Le traitement primaire des D3E dans le secteur formel comprend généralement des opérations de tri manuel ou automatisé et de démantèlement des appareils, lesquelles peuvent s'accompagner de broyage ou d'éclatement afin d'en séparer les différents composants à revaloriser et à acheminer vers des recycleurs secondaires (fonderies de métal, fabricants de produits en plastique ou en verre). Ces opérations peuvent libérer des particules dans l'air, provenant des appareils eux-mêmes ou encore des poussières enfermées et accumulées dans ceux-ci. Des analyses de l'air et des poussières déposées dans ce type d'industrie ont témoigné de la présence de composés ignifuges à des concentrations supérieures à celles retrouvées dans l'environnement ou dans d'autres milieux de travail, et qui présentent un grand potentiel d'exposition pour les travailleurs (Makinen et al. 2009; Rosenberg et al. 2011). Cependant, à l'échelle internationale, très peu d'études d'évaluation de l'exposition aux ignifuges ont été réalisées dans le secteur du recyclage électronique formel.

1.3.3. Expositions

Les ignifuges ne sont pas les seules substances qui sont retrouvées en grande concentration dans le recyclage électronique. Les métaux constituent une partie importante des D3E, en plus du plastique ; à titre d'exemple, les métaux et métalloïdes constituent en moyenne 23 % du poids d'un téléphone portable (Schluep et al. 2009). Les plus communs sont le cuivre, l'étain, l'antimoine, l'aluminium le cobalt, le plomb, le mercure, le cadmium et l'arsenic (Schluep et al. 2009). Ces substances peuvent être émises sous forme de particules ou de vapeurs (pour le mercure) lors des opérations de recyclage électronique. Des concentrations relativement élevées de plomb et de cadmium ont notamment été mesurées dans l'air des entreprises de recyclage électronique états-uniennes, soit jusqu'à plus de 50% des valeurs limites d'exposition professionnelle recommandées par l'American Conference of Governmental Industrial Hygienists (ACGIH) (Ceballos et al. 2014). Des études dans des installations de recyclage électronique suédoises (Julander et al. 2014) et françaises (Lecler et al. 2015) ont également mesuré des concentrations de plomb plus élevées que ce qui avait été mesuré dans des tours à bureaux, et parfois dépassant les valeurs limites d'exposition professionnelle selon la tâche effectuée.

Des études animales et *in vitro* ont révélé divers mécanismes par lesquels les métaux pouvaient altérer l'équilibre endocrinien. Il a notamment été montré en laboratoire que le cadmium avait une affinité pour les récepteurs estrogènes et qu'il pouvait bloquer la synthèse d'hormones stéroïdiennes comme la testostérone et la progestérone (De Coster and van Larebeke 2012; Takiguchi and Yoshihara 2006). Le plomb serait quant à lui associé à une diminution de la concentration sérique des hormones LH et FSH (Figa-Talamanca et al. 2001; Iavicoli et al. 2009). Dans un modèle porcin, le mercure aurait la capacité d'inhiber la production de progestérone par des cellules ovariennes et d'affecter la régulation de cette même hormone par le biais d'une inhibition de l'hormone de régulation FSH (Kolesarova et al. 2010; Roychoudhury et al. 2015). Les études épidémiologiques sont moins probantes, mais tendent à confirmer les observations faites chez les modèles animaux (Gore et al. 2015).

L'exposition à de nombreuses substances chimiques résultant du travail avec des D3E pose donc le problème d'effets possiblement synergiques ou additifs des mélanges complexes sur l'équilibre endocrinien. En particulier, les effets de l'exposition simultanée à plusieurs perturbateurs endocriniens, en l'occurrence des métaux et des ignifuges, n'ont été que très peu étudiés (Crofton 2008; Saunders et al. 2015; Wade et al. 2002a). Des chercheurs ont toutefois rapporté des relations dose-réponse complexes, où des synergies pouvaient apparaître en deçà ou au-delà d'un certain seuil théorique d'exposition, même si deux substances avaient un effet isolé sur les hormones en apparence antagoniste (De Coster and van Larebeke 2012). Une étude de toxicité chez des rats exposés à un mélange de composés organochlorés (dont certains ont des patrons moléculaires similaires à ceux des ignifuges chlorés) et de métaux (plomb et cadmium) a montré des altérations significatives au niveau des hormones thyroïdiennes, quoique d'une grande variabilité (Wade et al. 2002b). Jusqu'à maintenant, la recherche sur les effets endocriniens combinés d'une exposition aux métaux et aux ignifuges a principalement porté sur des analyses *in vitro* et chez les espèces animales, mais les résultats portent à croire que des effets additifs ou synergiques pourraient être observés aussi chez l'humain (Curcic et al. 2014; Li et al. 2010; Yu et al. 2015; Zhu et al. 2014).

1.4. Résumé des enjeux

Nous savons que les ignifuges sont pratiquement ubiquitaires dans l'environnement. Nous ignorons cependant à ce jour si certains sous-groupes de la population canadienne sont plus exposés que d'autres, comme par exemple les travailleurs de certaines industries. De plus, comme il n'existe pas de valeur limite d'exposition professionnelle pour les ignifuges, il serait important de connaître le niveau d'exposition de base dans la population pour disposer d'un niveau de référence permettant d'estimer la contribution de la contamination dans certains milieux de travail à l'exposition des travailleurs.

Différentes études rapportent des niveaux d'exposition aux ignifuges dans des milieux de travail, par le biais de mesures dans l'air ou encore d'indicateurs biologiques. Il n'y a cependant pas de compilation systématique de ces données qui faciliterait l'identification des milieux les plus exposants.

Puisque les ignifuges sont très présents dans les équipements électroniques, l'industrie du recyclage électronique constitue un milieu de prédilection pour étudier l'exposition des travailleurs. De plus, cette industrie est en croissance au Québec et il est important d'y mesurer dès maintenant les niveaux d'exposition dans une perspective préventive.

Finalement, les ignifuges sont soupçonnés d'avoir des propriétés toxiques pour le système endocrinien. Cependant, les études sont discordantes et plusieurs sont effectuées chez des sujets peu représentatifs de la population de travailleurs, dont le choix limite la validité externe des résultats, par exemple des hommes soignés dans une clinique de fertilité ou encore des femmes enceintes. Il importe d'effectuer ce type d'étude chez un groupe de sujets qui a le potentiel d'être exposé au-delà des limites de détection, et qui idéalement n'a pas de condition majeure qui puisse influencer ses niveaux d'hormones.

1.5. Objectifs

1.5.1. Objectif général

L'objectif général de cette thèse est d'évaluer l'exposition à des ignifuges chez les travailleurs du recyclage et d'étudier les effets endocriniens associés.

1.5.2. Objectifs spécifiques

1) Le premier objectif est de déterminer le niveau d'exposition des travailleurs canadiens et états-uniens aux ignifuges polybromodiphényléthers à l'aide de données populationnelles.
2) Le second objectif est d'identifier les milieux de travail où l'exposition aux ignifuges est la plus importante, et d'en compiler les niveaux.
3) Le troisième objectif est d'évaluer l'exposition d'une population québécoise de travailleurs du recyclage électronique aux groupes d'ignifuges les plus communs et d'identifier les déterminants de cette exposition.
4) Le quatrième objectif est d'explorer les effets endocriniens associés à une exposition concomitante à plusieurs ignifuges, de même qu'aux métaux, chez un groupe de travailleurs du recyclage électronique.

1.6. Organisation de la thèse

Cette thèse se présente en sept chapitres. Le premier présente une mise en contexte, l'état des connaissances, de même que les objectifs de la thèse. Le second chapitre décrit les méthodes employées pour répondre aux objectifs. Les quatre chapitres suivants consistent en quatre manuscrits d'articles scientifiques, constituant le corps de cette thèse. Le chapitre 7 résume les principaux résultats des chapitres précédents, comprend une discussion générale des résultats, ainsi que la conclusion de la thèse.

Les quatre articles sont ceux-ci :

1) Gravel S, Lavoué J, Labrèche F. 2018. Exposure to polybrominated diphenyl ethers (PBDEs) in American and Canadian workers: Biomonitoring data from two national surveys. Science of the Total Environment; 631-632:1465-1471.
2) Gravel S, Aubin S, Labrèche F. 2019. Assessment of Occupational Exposure to Organic Flame Retardants: A Systematic Review. Annals of Work Exposures and Health; 63(4):386-406.
3) Gravel S, Lavoué J, Bakhiyi B, Diamond ML, Jantunen L, Lavoie J, Roberge B, Verner M-A, Zayed J, Labrèche F. 2019. Halogenated flame retardants and organophosphate esters in the air of electronic waste recycling facilities: Evidence of high concentrations and multiple exposures. Environment International; 128:244-253.
4) Gravel S, Lavoué J, Bakhiyi B, Lavoie J, Roberge B, Patry L, Bouchard M, Verner M-A, Zayed J, Labrèche F. 2020. Multi-exposures to suspected endocrine disruptors in electronic waste recycling workers: associations with thyroid and reproductive hormones. International Journal of Hygiene and Environmental Health; 225. (sera publié dans le numéro d'avril)

1.7. Positionnement et contribution de l'étudiante dans le projet de recherche

Tel que mentionné précédemment, cette thèse est associée à un projet financé par l'IRSST, intitulé « Évaluation de l'exposition aux contaminants chimiques des travailleurs œuvrant dans le recyclage primaire des matières résiduelles électroniques au Québec et appréciation du risque sanitaire (Projet 2015-0083) » dont les chercheurs principaux sont Joseph Zayed et France Labrèche. Il s'agit d'une recherche de trente mois dont l'objectif principal est d'évaluer l'exposition des travailleurs aux métaux et aux ignifuges dans le secteur de l'e-recyclage primaire au Québec et d'apprécier le niveau de risque sanitaire en découlant. L'étudiante a contribué à la rédaction du devis de recherche de l'ensemble du projet. Elle a également participé activement à la préparation du matériel, au recrutement des travailleurs ainsi qu'à la collecte de données sur le terrain (air, matrices biologiques et questionnaires) en collaboration avec les techniciens et chercheurs du projet. L'étudiante a préparé les échantillons biologiques au laboratoire de toxicologie de l'IRSST avant leur analyse, de même qu'assuré les envois des échantillons aux laboratoires d'analyse externes, le cas échéant. L'étudiante a recueilli les données auprès des laboratoires, préparé la base de données, procédé aux analyses statistiques, et rédigé la première version de chaque manuscrit.

1.7.1. Présentations comme première auteure découlant du projet

L'étudiante a eu l'occasion de présenter différents résultats préliminaires dans plusieurs congrès nationaux et internationaux au cours de ses études doctorales. En voici la liste :

Présentations orales

Gravel, S., Diamond, M. L., Jantunen, L., Verner, M.-A., Zayed, J., & Labrèche, F. (2019). Are airborne concentrations of BDE209 associated with serum concentration in recycling workers? Présenté au 9th International Symposium on Flame Retardants (BFR), Montreal, Canada.

Gravel, S., Bakhiyi, B., Lavoué, J., Verner, M.-A., Zayed, J., & Labrèche, F. (2019). Electronic waste recycling exposure and hormone levels in workers. Présenté au symposium EPICOH 2019, Wellington, New-Zealand. (préparée par SG, présentée par FL)

Gravel, S., Bakhiyi, B., Diamond, M. L., Jantunen, L. M., Lavoie, J., Nguyen, L. V., . . . Labrèche, F. (2018). Recycling is not all green: Workers' exposure to metals and flame retardants in Quebec e-recycling facilities. Présenté au congrès 2018 de l'Association canadienne de recherche en santé au travail (ACRST), Vancouver, BC.

Gravel, S., Bakhiyi, B., Lavoie, J., Roberge, B., Verner, M.-A., Zayed, J., & Labrèche, F. (2018). Electronic waste recycling in Canada - Biomonitoring of workers' exposure to flame retardants. Présenté au congrès 2018 de l'Association canadienne de recherche en santé au travail (ACRST), Vancouver, BC.

Gravel, S., Lavoué, J., & Labrèche, F. (2017). Workers' exposure to brominated flame retardants: A glance at American and Canadian population databases. Présenté au symposium EPICOH 2018, Edinburgh, Scotland.

Présentations par affiche

Gravel, S., Bakhiyi, B., Bernstein, S., Diamond, M., Jantunen, L., Lavoie, J., . . . Labrèche, F. (2018). E-waste recycling in Canada – workers' exposure to metals and flame retardants. Présenté au ICOH International Congress 2018, Dublin, Ireland.

Gravel, S., Lavoué, J., & Labrèche, F. (2017). Industry, occupation and sex differences in workers' exposure to endocrine disrupting metals in an American and a Canadian survey. Présenté au symposium EPICOH 2017, Edinburgh, Scotland.

Chapitre 2. Méthodologie

Ce chapitre présente les approches méthodologiques utilisées pour atteindre les objectifs de la thèse. Dans un premier temps, les types de données étudiées sont présentés, soit les données d'enquêtes populationnelles, une revue de littérature des données d'exposition, ainsi que des données nouvelles acquises sur le terrain dans des entreprises québécoises. Par la suite, ce chapitre se penche sur les méthodes statistiques particulières qui sont employées dans les articles de la thèse. On y voit notamment les modèles Tobit, la régression à risques proportionnels de Cox inversée, et finalement, l'analyse en composantes principales.

2.1. Données utilisées

2.1.1. Données d'enquêtes populationnelles

Tel que mentionné précédemment, il existe peu de données d'exposition aux ignifuges dans la population générale adulte, et encore moins chez des groupes de travailleurs. Pourtant, en l'absence de valeurs limites d'exposition professionnelle, de telles données sont nécessaires pour atteindre le premier objectif de la thèse. Deux bases de données populationnelles ont été analysées pour en dégager les valeurs d'exposition de base chez les travailleurs adultes canadiens et états-uniens.

La seule base de données populationnelle canadienne qui comprend des mesures biologiques d'ignifuges est l'Enquête canadienne sur les mesures de la santé (ECMS). Cette enquête biennale menée par Statistique Canada vise à recueillir des données sur l'état de santé et les habitudes de vie d'un échantillon représentatif de la population canadienne. Dans le premier cycle de l'enquête, soit pour les années 2007-2009, un sous-groupe de la population participante a fourni un échantillon de sang dans lequel des congénères de PBDE ont été mesurés. Ces données sont accessibles par l'intermédiaire d'un serveur sécurisé dans des locaux réservés aux employés de Statistique Canada. Un chercheur intéressé à ces données doit compléter une demande d'accès et sera ensuite considéré comme un employé de Statistique Canada, c'est-à-dire qu'il doit se soumettre à des règles de diffusion des résultats qui permettent de conserver l'anonymat des participants. De plus, tous les résultats d'analyse produits doivent être révisés par un analyste avant de quitter les locaux. Ces données populationnelles présentent certaines limites particulières dans le cadre du présent projet.

Notamment, l’industrie où les participants travaillent est classée selon les 20 grands secteurs industriels du Système de classification des industries de l'Amérique du Nord (SCIAN), selon un niveau de précision limité. De plus, les valeurs limites de détection des analytes sont relativement élevées, ce qui occasionne un grand pourcentage de valeurs non détectées. Ensuite, le BDE209 n’a pas été mesuré, puisque les données ont été recueillies il y a plus de 10 ans, alors que les méthodes analytiques n’étaient pas au point pour ce congénère. Néanmoins, il s’agit à ce jour des données canadiennes les plus complètes pour estimer les niveaux de base des biomarqueurs d’exposition aux PBDE.

La base de données états-unienne National Health and Nutrition Examination Survey (NHANES) est très similaire à celle de l’ECMS, et comprend des mesures de PBDE sérique pour le cycle d’enquête 2003-2004, mais elle aussi sans résultats pour le congénère BDE209. Ces données sont disponibles sous forme anonymisée en libre accès sur le web. Les limites de ces données sont sensiblement les mêmes que pour l’ECMS, à l’exception que l’âge minimal dans le sous-échantillon PBDE est de 16 ans alors qu’il est de 20 ans pour l’enquête canadienne. Au moment de la préparation de l’article 1 (chapitre 3), aucune de ces deux bases de données ne contenait des valeurs d’exposition pour d’autres groupes chimiques d’ignifuges, comme les OPE ou encore les NBFR.

La comparaison de deux bases de données limite la complexité d’analyse possible parce qu’il n’est possible de retenir que les variables communes aux deux bases et codifiées de façon similaire. Par conséquent, il n’a pas été possible d’étudier plus précisément les variables relatives à l’ethnie ou à l’éducation, par exemple.

2.1.2. Revue de la littérature

En général, certains contextes professionnels semblent exposer les travailleurs à des concentrations d’ignifuges au-delà des niveaux d’exposition environnementale. Il n’existe cependant pas encore de recension systématique des articles qui ont évalué l’exposition à ces substances en milieu de travail. Un tel recueil est utile pour comparer les différents milieux et mettre en évidence ceux où les expositions sont plus élevées. De plus, certains problèmes méthodologiques paraissent récurrents dans la littérature, mais aucune évaluation critique concernant les méthodes d'évaluation de l'exposition professionnelle aux ignifuges n'a été publiée. Pourtant, une telle appréciation peut être utile pour la sélection d'approches appropriées et reproductibles pour des prélèvements sur le terrain. Une revue systématique de la littérature doit elle-même suivre une méthodologie rigoureuse afin d'être exhaustive et reproductible, ce qui est présenté dans ce qui suit.

La consultation de différents moteurs de recherche bibliographique augmente les chances de repérer exhaustivement les articles publiés sur un sujet donné. Bramer et al. (2017) proposent, pour le domaine médical, une combinaison de bases de données qui optimise la recherche de références dans un but de revue systématique. Ces auteurs considèrent de consulter minimalement les bases Embase, MEDLINE, Web of Science Core Collection, ainsi que Google Scholar afin de couvrir un nombre adéquat et efficace de publications. Il est avisé de consulter également les bibliographies d'articles clés sur le sujet pour identifier quelques publications ayant échappé à la recherche.

Les résultats de la revue systématique ont été présentés selon l'énoncé PRISMA, ou *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (Items préférés pour rendre compte des revues systématiques et des méta-analyses). PRISMA est constitué de deux composants (Moher et al. 2009) : le premier consiste en un organigramme indiquant le nombre d'articles identifiés, inclus et exclus, ainsi que les raisons des exclusions. Le second est une liste de 27 éléments à observer, à l'intérieur des sections Titre, Résumé, Méthodes, Résultats, Discussion et Financement, pour rapporter les résultats à l'aide de critères scientifiques. L'endroit dans le texte renseignant chacun des items doit être indiqué dans un tableau fourni en annexe. L'utilisation de cet énoncé facilite l'évaluation de la conduite d'une revue de littérature selon des critères standardisés faisant l'objet d'un consensus.

2.1.3. Acquisition de données nouvelles : le projet IRSST

Le projet de l'IRSST avait pour but d'évaluer l'exposition des travailleurs aux contaminants chimiques (métaux et ignifuges), d'apprécier le niveau de risque sanitaire et de documenter les pratiques de santé et de sécurité au travail (SST) dans le secteur du recyclage électronique primaire au Québec. Les objectifs spécifiques étaient :

1) de décrire les différentes opérations et procédés de travail dans l'industrie du recyclage électronique;
2) de documenter les pratiques de gestion de la SST mises en œuvre dans le milieu du recyclage électronique;
3) d'évaluer l'exposition des travailleurs aux métaux et aux agents ignifuges;
4) d'explorer la présence d'effets précoces à la santé en ce qui concerne la perturbation endocrinienne (plus spécifiquement des hormones thyroïdiennes et reproductives);
5) d'apprécier le risque potentiel pour la santé des travailleurs en fonction des niveaux d'exposition qui auront été mesurés.

Les sections suivantes présentent le devis de l'étude menée pour atteindre ces objectifs, tout en considérant que le travail de thèse concerne plus particulièrement les objectifs 2, 3, et 4.

Recrutement des entreprises

Il était prévu de recruter des entreprises de recyclage électronique situées autour de la région de Montréal pour faciliter les déplacements sur le terrain et la gestion des échantillons après la journée de prélèvement, tout en obtenant un échantillon vraisemblablement caractéristique des différents types d'entreprises de recyclage électronique au Québec. Il y a dans la province deux grands types d'entreprises de recyclage électronique : des entreprises privées et des entreprises à but non lucratif, ces dernières ayant une mission d'aide à l'emploi pour des personnes en réinsertion sociale ou encore des personnes souffrant d'un handicap.

Le choix du groupe de comparaison a posé un défi de taille. Comme les groupes chimiques d'ignifuges étudiés sont fréquemment rencontrés dans la majorité des milieux de travail (Abbasi et al. 2016; Brommer and Harrad 2015; Stapleton et al. 2008), nous désirions obtenir un groupe pour lequel seulement l'exposition chimique était différente de celle des travailleurs du recyclage électronique. L'industrie du recyclage commercial (verre, carton, métal) a donc été ciblée. Ce genre d'entreprise fait appel à une main-d'œuvre dont il est fort probable que le statut socio-économique soit similaire à celui des travailleurs du recyclage électronique (Lavoie and Guertin 1999; Poulsen et al. 1995). Il est certes possible que les travailleurs y soient tout de même exposés à différents perturbateurs endocriniens, mais dans une moindre mesure que dans le recyclage électronique. De plus, la signature des différents groupes chimiques d'ignifuges identifiés à la fois dans l'air et dans les liquides biologiques des travailleurs est présumée différente dans ces deux industries, telle qu'observée ailleurs dans d'autres industries (Hearn et al. 2013).

Des entreprises de recyclage électronique ont été identifiées à partir d'une recherche internet. Une vingtaine d'entreprises ont été approchées, et les responsables de neuf d'entre elles ont accepté de participer à la suite d'une rencontre face à face. Sur ces neuf entreprises, deux ont fermé ou changé de vocation avant la campagne de prélèvements et la troisième a été jugée trop éloignée de la région de Montréal. Quant au groupe de comparaison, une dizaine d'entreprises de recyclage domestique ou commercial ont été contactées et une seule a accepté de participer.

Recrutement des travailleurs

Le principal critère d'inclusion quant au choix des travailleurs du recyclage était d'être en présence quasi continuelle de D3E ou de déchets d'autre nature, soit par les tâches de tri et de démantèlement manuelles, d'opération de compacteurs ou autre machinerie, ou encore par des tâches de supervision.

Le recrutement des participants a été effectué selon les étapes suivantes :

1) Rencontre de groupe avec les travailleurs, explication des diverses étapes du projet, réponse aux questions et remise du formulaire de consentement et du feuillet d'information.
2) Identification des travailleurs intéressés à participer lors de la première rencontre et dans les jours suivants. Les travailleurs intéressés devaient répondre à quelques questions afin de déterminer leur éligibilité (voir critères d'inclusion et d'exclusion dans l'article 4 (chapitre 6).
3) Rencontre individuelle avec chacun des travailleurs pour la signature des formulaires de consentement le matin de la première journée d'échantillonnage.

Le projet a été présenté à plus de 150 travailleurs. Quatre-vingt-huit travailleurs ont été recrutés dans des entreprises de recyclage électronique primaire et constituent le groupe exposé. Le groupe de comparaison est constitué de dix travailleurs provenant d'une entreprise de recyclage commercial, et de cinq travailleurs d'une entreprise de recyclage électronique ayant une division « recyclage du papier ».

Les participants se sont vu offrir une compensation financière de cent dollars. Ceci visait à les dédommager pour la participation à l'étude hors des heures de travail régulières et pour l'inconfort relatif à leur participation à l'étude (port de pompe personnelle, recueil de leur urine et prise de sang).

Considérations éthiques

Le protocole du projet IRSST et le formulaire d'information et de consentement ont été approuvés par le Comité d'éthique de la recherche en sciences et en santé de l'Université de Montréal. Pour assurer le caractère confidentiel et anonyme des données, chaque participant n'a été identifié qu'avec un code dont seuls les chercheurs coresponsables de la recherche détiennent la clé. Chacun des travailleurs participants a signé librement un formulaire de consentement éclairé. De plus, un médecin de la Clinique de médecine du travail et de l'environnement du Centre hospitalier de l'Université de Montréal, co-chercheur du projet, a revu les résultats biologiques des travailleurs (tant pour les hormones que pour les métaux sanguins ou urinaires) de façon à assurer un suivi médical au besoin. Lorsque certains résultats de métaux ont atteint le seuil de déclaration au directeur de la santé publique selon la Loi sur la santé publique et ses règlements (Gouvernement du Québec 2019a), le laboratoire d'analyse a procédé à une déclaration nominale aux autorités de santé publique concernées.

Déroulement de la collecte de données

Deux jours de prélèvement par entreprise ont été requis : le jour 1 pour tous les ignifuges dans l'air et les métabolites d'OPE dans l'urine, ainsi que le jour 2 pour les métaux dans l'air, l'urine et le sang, de même que les ignifuges PBDE et les hormones dans le sang (Tableau 2.1). Des questionnaires ont également été complétés à la fin de la seconde journée de prélèvement, et l'enquête d'hygiène s'est échelonnée sur les deux jours. Cette dernière a consisté en l'observation de tous les travailleurs par une hygiéniste du travail certifiée, afin de recenser les pratiques de travail et d'hygiène des participants. Des échantillons d'air ont été prélevés dans la zone respiratoire des travailleurs pour les ignifuges et les métaux, sélectionnés sur la base de leur présence dans les résidus des D3E, de leur toxicité endocrinienne potentielle, de même que sur leur détection dans des entreprises de recyclage électronique hors Québec.

Les échantillons d'urine pour les ignifuges organophosphorés ont été prélevés à la fin de la journée de travail de manière à refléter l'exposition de la journée pour ces substances dont la demi-vie est de quelques heures (Hou et al. 2016). Quant aux échantillons de sang pour les PBDE, ils ont été prélevés à la fin de la journée de travail, vers la fin de la semaine (jeudi), de manière à refléter l'exposition de la semaine pour les congénères à plus courte demi-vie comme le BDE209 (Geyer et al. 2004; Thuresson et al. 2006b). Les échantillons de sang pour la mesure des hormones sont prélevés vers la même heure en fin de journée pour tous les participants, de manière à limiter l'effet des variations diurnes (Brambilla et al. 2009).

Tableau 2.1. Détail de la collecte de données et d'échantillons

Donnée	Jour 1	Jour 2
Air, poste personnel	40 ignifuges	12 métaux
Air, poste fixe	2 métaux Matières particulaires totales	2 métaux Matières particulaires totales
Urine	15 ignifuges OPE	6 métaux
Sang	-	3 métaux 12 ignifuges PBDE 10 hormones
Entrevue	Formulaire de consentement	Questionnaire
Pratiques de travail	Enquête d'hygiène	Enquête d'hygiène

2.2. Méthodes statistiques

2.2.1. Régression sur des jeux de données censurées

Toute analyse de substances dans l'air ou dans les matrices biologiques comporte des limites de détection analytique. Les valeurs rapportées par les laboratoires comme « sous la limite de détection (LOD) » ou encore « sous la limite de quantification (LOQ) » sont dites « censurées à gauche », c'est-à-dire qu'on ne connaît d'elles que le fait qu'elles sont quelque part entre zéro et la LOD (ou LOQ) (Helsel 2010). Si une faible proportion (autour de 15% et moins) des valeurs du jeu de données est sous la LOD, une substitution simple des valeurs par la LOD divisée par 2 ou par la racine carrée de 2 peut produire une estimation acceptable lors de l'estimation de paramètres distributionnels comme la moyenne arithmétique ou géométrique (Hornung and Reed 1990) ou encore dans des analyses multivariées (Lubin et al. 2004). Cependant, lorsqu'une grande proportion des valeurs sont censurées (au-delà de 50%), il est préférable d'employer d'autres méthodes pour obtenir des estimations fiables, comme les modèles Tobit ou les approches bayésiennes (Hewett and Ganser 2007; Huynh et al. 2016). Ceci est particulièrement important dans le cadre de tests statistiques formels, quoique ces méthodes présentent des prémisses parfois contraignantes, comme les modèles Bayesiens et Tobit qui requièrent une hypothèse de distribution, et ce dernier qui requiert l'indépendance du terme d'erreur (où la variance ne dépend pas de la variable indépendante du modèle). Bien que les mesures environnementales soient généralement distribuées selon la loi log-normale (Kromhout 1994; Rappaport and Kupper 2011), la nature hétérogène des activités de travail et du matériel traité dans le recyclage électronique peut résulter en des distributions inhabituelles. Il peut être intéressant alors d'avoir recours à certaines méthodes statistiques qui ne requièrent pas de distribution préalable, et dont les prémisses ne requièrent pas l'homogénéité des variances. Ces méthodes, soit les modèles Tobit et la régression de Cox inversée, appuyés sur des prémisses différentes, ont été utilisées dans cette thèse et sont décrites dans les pages qui suivent.

Les modèles Tobit (articles 3 et 4, respectivement chapitres 5 et 6)

Les modèles Tobit consistent en une régression censurée, c'est-à-dire qu'elle permet d'estimer une relation linéaire entre une variable réponse et une variable explicative, lorsque la valeur de cette dernière est en partie censurée (Tobin 1958). Cette méthode s'utilise lorsque les données sont censurées à droite de la distribution (perte de vue dans une enquête), ou à gauche comme en présence de valeurs de concentration de substances sous la limite de détection analytique (Lubin et al. 2004).

Le modèle suppose une variable latente y^*, laquelle est inobservable sous une valeur de censure τ (McDonald and Moffitt 1980). Soit y la variable observée, elle est fixée à τ_y (la limite de détection) si la variable latente se situe sous τ :

$$y = \begin{cases} y^* \; si \;\; y^* > \tau \\ \tau_y \; si \;\; y^* \leq \tau \end{cases}$$

L'équation du modèle comprenant un seul coefficient (comme dans le cas d'une régression linéaire simple) est ainsi $y_i^* = X_i\beta + \varepsilon_i$. Le modèle Tobit emploie le calcul de la vraisemblance maximale (maximum likelihood) pour produire une estimation du coefficient β à partir de l'ensemble des observations i et des valeurs associées du prédicteur X_i*;* et où le terme des résidus ε_i est indépendant et distribué selon la loi normale (Holden 2004; McDonald and Moffitt 1980). Le coefficient β estime l'augmentation linéaire de la variable latente pour chaque augmentation d'unité de X. Par exemple, dans un modèle Tobit où l'on veut estimer l'effet de l'ancienneté en mois sur la concentration d'un ignifuge, un β de 2,0 s'interprète comme une augmentation de 2 ng/m³ pour chaque mois d'ancienneté. Les données censurées sont prises en compte par le fait que la vraisemblance pour ces observations est calculée selon une équation différente de celle utilisée pour les données observées.

La régression à risques proportionnels de Cox inversée (article 3, chapitre 5)

La régression à risques proportionnels de Cox (*Cox proportional hazard regression*; RRPC) est habituellement employée dans un contexte d'exposition et d'effet pour lequel le temps est un facteur important. Elle permet de calculer le risque de survenue d'un événement, considérant la survie d'un sujet jusqu'au moment de cet événement (Rothman et al. 2008;

Szklo and Nieto 2012). La mesure d'effet calculée est ainsi un ratio de probabilités (hazard ratio), où l'on peut comparer la probabilité de survenue d'un événement entre différents groupes. Par exemple si l'on compare, entre les hommes (groupe de référence) et les femmes, la durée en années entre l'embauche et la démission (événement) dans le département d'une entreprise, et que le coefficient calculé est de 2, cela signifie que l'on peut s'attendre à deux fois plus de démissions par années chez les femmes que chez les hommes.

En plus du temps jusqu'à la survenue d'un événement (par exemple, la démission d'un travailleur), la RRPC tient compte de la perte de vue des sujets (par exemple, sa mutation dans un autre département). Ces deux types d'événements peuvent se produire à différents moments, mais la perte de vue est considérée comme étant une censure des données à droite de la distribution, où elle est nécessairement antécédente à l'événement d'intérêt pour un sujet donné (Cox 1972). De plus, cette approche présuppose que la probabilité de survenue de l'événement est proportionnelle à une probabilité de base; c'est-à-dire que les rapports de risque (hazard ratio ou relative hazard) comparant différents groupes entre eux ne changent pas avec le temps et demeurent proportionnels. Ainsi, le risque d'un groupe donné $h_1(t)$ au temps t est le multiple d'un risque de base $h_0(t)$ et du ratio de probabilités, lequel est une expression exponentielle de la combinaison linéaire des variables prédictives : $h_1(t) = h_0(t)\ exp(\beta_1 x_1 + \ldots + \beta_k x_k)$, où $x_1 \ldots x_k$ sont des covariables indépendantes (Rosner 2010; Szklo and Nieto 2012). Selon t, les risques $h_1(t)$ et $h_0(t)$ peuvent donc indépendamment changer, mais le ratio $\frac{h1(t)}{h0(t)}$ ne change pas (Machin et al. 2006). La RRPC est une méthode statistique semi-paramétrique, parce que seules les variables indépendantes sont paramétrées et appartiennent à une distribution déterminée, et non la variable de temps t qui elle ne requiert pas de distribution particulière.

Puisque la censure est prise en compte dans la RRPC, il est possible d'utiliser cette approche statistique avec des données d'exposition qui comprennent des valeurs sous la LD où ces données censurées à gauche sont transformées pour être reportées à droite. La transformation consiste à soustraire chaque résultat d'une valeur égale ou supérieure à la valeur maximale mesurée de la distribution, de manière à renverser la distribution (Helsel 2012). Alors, pour une valeur maximale M, une concentration mesurée T et une valeur transformée t; cette dernière est représentée par t = M – T, où la vraie concentration maximale deviendra 0 et où les valeurs sous la limite de détection s'approcheront de M. De cette manière, la variable de concentration fait office de variable temporelle t dans la régression de Cox, et la variable indépendante x peut être un déterminant catégorique ou continu de l'exposition (ou encore une issue de santé) (Dinse et al. 2014). Cette utilisation de la méthode est nommée « régression à risques proportionnels de Cox inversée » (*reverse-scale Cox's proportional hazard regression*) (Dinse et al. 2014).

L'interprétation du rapport de risque issu d'une RRPC inversée doit se faire avec prudence. Dans le cas d'une variable indépendante binaire (p. ex. travailleur permanent ou temporaire), un rapport de risques ainsi obtenu peut s'interpréter comme un rapport de cotes (odds ratio). Le rapport de cotes pour une variable binaire représente le quotient entre la cote pour un groupe d'avoir une concentration plus élevée que la concentration t, sur la cote pour l'autre groupe d'avoir une concentration plus élevée que la concentration t. Ainsi, en comparant le risque à une concentration t pour un déterminant de l'exposition où x=0 est le groupe « travailleurs permanents » et x=1 est le groupe « travailleurs temporaires », le risque pour les travailleurs permanents à la concentration t s'exprime [$h_0(t)$], et le risque cumulatif pour les travailleurs temporaires à t s'exprime [$H_0(t)$]; le odds ratio s'exprime donc [$h_0(t)$/ $H_0(t)$] / [h_1(t)/ $H_1(t)$]. Par exemple, un coefficient de régression de Cox pour les travailleurs temporaires de 0,4 correspond à un ratio de probabilités de $e^{(0.4)}$ = 1,5, ce qui signifie que les travailleurs temporaires auraient une probabilité 50 % fois plus grande d'avoir une exposition plus élevée que les travailleurs permanents. Dans le cas où x est continu, il s'agit d'un ratio de probabilités pour un changement de une unité de x (Dinse et al. 2014). Ainsi, contrairement à aux modèles Tobit où l'on estimerait le ratio des niveaux moyens d'exposition, on estime ici le ratio de la probabilité d'être plus exposé.

Puisque cette approche requiert que le ratio de probabilités soit constant sur les différentes concentrations de contaminants (t), il est important de vérifier cette supposition en testant la signification statistique du modèle auquel on ajoute le produit d'une variable d'intérêt x et de la concentration t. Dans le cas où cette supposition est enfreinte, il est plus prudent de présenter les résultats selon différentes fourchettes de t (Rosner 2010). Cette méthode a toutefois l'avantage de ne pas requérir de suppositions relatives quant à la distribution de la variable de concentration t.

2.2.2. Analyse en composantes principales

L'analyse de l'exposition à un mélange de plusieurs substances est une problématique rencontrée fréquemment en santé environnementale et en santé au travail (Roberts and Martin 2006). Les substances, en plus d'être nombreuses, ont également des chances d'être corrélées, et il pourrait être intéressant d'observer les profils d'exposition pour identifier des groupes de substances plus susceptibles de se retrouver en concentration élevée ensemble. L'analyse en composantes principales permet, en réduisant le nombre de variables observées, d'illustrer les profils tout en diminuant la dimensionnalité du jeu de données. De plus, la régression sur les composantes principales (RCP) représente une avenue intéressante pour analyser les effets d'une multiexposition, généralement observée dans le recyclage électronique.

Analyse en composantes principales (article 4, chapitre 6)

L'analyse en composantes principales (ACP) a pour but de simplifier un jeu de données comprenant de nombreuses variables prédictives, lesquelles peuvent être colinéaires (Lever et al. 2017). Elle permet toutefois de préserver les tendances et la structure du jeu de données. Cette méthode s'avère une avenue intéressante pour étudier les données environnementales où plusieurs contaminants sont prélevés et sont corrélés entre eux.

L'ACP réduit les données en trouvant le meilleur « résumé » géométrique constitué du plus faible nombre de composantes vectorielles possible, tout en préservant le maximum de variance. Tel qu'illustré sur la Figure 2.1a pour une base de données à deux variables x et y, l'ACP consiste à projeter ces données en deux dimensions (axes x et y) sur un plan à une seule dimension (axe u), de manière à ce que la variance sur u soit optimale. La Figure 2.1b montre les points sur l'axe x et sur l'axe y où leur variance est de 1, puis leur projection sur deux composantes, soit u et v. On constate que les points projetés sur la composante u ont une variance de 1,78, alors que s'ils sont projetés sur l'axe v, ils ont une variance plus faible. La composante u est donc celle qui optimise la variance des données. Pour un jeu de données à plusieurs variables, les composantes subséquentes sont sélectionnées de la même manière, mais doivent être non corrélées avec les autres, c'est-à-dire orthogonales. Ceci résulte en un nombre de composantes total qui correspond au plus petit nombre entre le nombre de variables et le nombre d'observations. Chaque variable d'un jeu de données se voit ainsi attribuer un score global pour chacune des composantes créées. Puisque les premières composantes capturent généralement une bonne proportion de la variance, il est possible par la suite de reporter le score de chaque variable sur un graphique dont les axes sont constitués de ces composantes (Figure 2.1c). Des profils d'exposition peuvent alors émerger et témoigner des co-expositions dominantes. Un des avantages majeurs de l'ACP est que les données n'ont pas besoin de présenter une quelconque distribution, pour autant que la structure soit linéaire (Jolliffe and Cadima 2016; Lever et al. 2017).

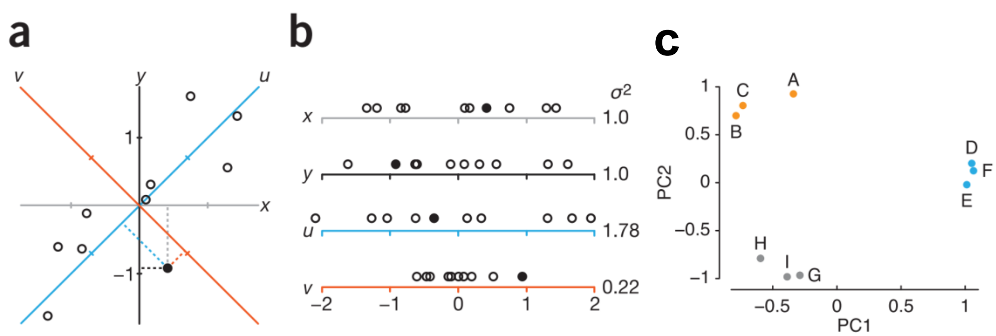


Figure 2.1. L'ACP projette des données 2D sur un plan 1D.
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Chapitre 3. Exposure to polybrominated diphenyl ethers (PBDEs) in American and Canadian workers: Biomonitoring data from two national surveys.

Exposure to polybrominated diphenyl ether (PBDE) in American and Canadian workers: biomonitoring data from two national surveys

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Cet article permet de répondre au premier objectif de la thèse. On y présente les niveaux d'exposition de la population de travailleurs canadiens et états-uniens aux PBDE afin d'établir le niveau d'exposition de base de la population. Cet article s'appuie sur les résultats de deux enquêtes populationnelles nationales.

L'étudiante a rédigé la demande d'accès à la base de données ECMS auprès de Statistique Canada. La base de données américaine NHANES est pour sa part disponible sur le web au www.cdc.gov/nchs/nhanes/. L'étudiante a procédé aux analyses statistiques, à l'interprétation des résultats, de même qu'à la rédaction du manuscrit et à sa révision jusqu'à sa publication. Le manuscrit a été révisé et approuvé par tous les co-auteurs.

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3.1. Abstract

Polybrominated diphenyl ethers (PBDEs) are flame retardants commonly found in many household and industrial products. They can be detected in the serum of the general population, and in even higher concentrations in workers of certain industries, due to an additional occupational exposure. The purpose of this analysis is to determine background exposure levels of PBDEs in the general working population, using national surveys where working status was self-reported. Participants aged 20-65 were selected from the 2003-2004 U.S. National Health and Nutrition Examination Survey (n=1141) and the 2007-2009 Canadian Health Measures Survey (n=1337). Only four congeners were detected in at least 25% of samples for both surveys: BDE47, 99, 100 and 153. NHANES workers had a geometric mean (GM [95% C.I.]) BDE47 concentration of 20.9 ng/g lipids [19.3, 22.7], and CHMS workers, 11.4 ng/g lipids [10.8, 12.1]. PBDE levels were not statistically significantly different between workers and non-workers, except for BDE153 in CHMS. Among workers, women had a significantly lower concentration of BDE153 than men in both surveys (%change [95% C.I.] with 1 ng/g lipid increase: -33.4% [-49.0, -12.9] in NHANES, -18.8% [-27.5, -8.9] in CHMS), in regressions adjusted for age, body mass index, smoking status, ethnicity and education. CHMS workers in the *Information, finance, real estate, and education* industry group had significantly higher BDE47 concentrations than non-workers. These results indicate a high exposure to PBDEs in two North-American countries, compared to data from other national surveys. The heterogeneity of the data did not permit a clear-cut distinction between workers and non-workers. Sex differences noted with BDE153 are consistent with those reported in other human exposure assessments and animal studies. Overall, industry-specific concentrations showed no particular pattern across both surveys. Despite some limitations, these data provide a useful estimate of the background exposure to PBDEs in American and Canadian workers.

3.2. Introduction

Flame retardants are used in various industrial and household materials, from textiles to plastics, building products, furniture and so on. Rather than being chemically bound to the materials, some flame retardants are mixed within and can be released in the air and dust as a result of materials' handling and aging (Coelho et al., 2014; Shoeib et al., 2012). Amongst the most commonly used, congeners of polybrominated diphenyl ethers (PBDEs) have been introduced as commercial mixtures in the fabrication process of electric and electronic devices, foam padding and insulation, and various fabrics since the 1970s (Vonderheide et al., 2008). Because of their reproductive toxicity and their potential for bioaccumulation, some commercial PBDE mixtures like Penta- or OctaBDE have undergone a voluntary phase-out in some countries, but they can still be found in the older products in which they were introduced; in addition, old and novel flame retardant mixtures are still being produced and added to imported and exported goods like smartphones and computers, to name only a few (Dodson et al., 2012; Turner and Filella, 2017).

Because of their ubiquity, PBDE congeners can be detected in the serum of the general population. They are generally measured in higher concentration in children and in older adults, presumably because of hand-to-mouth behavior and associated dust ingestion for the former, and bioaccumulation for the latter (Sjödin et al., 2008). Contrary to other persistent organic pollutants, PBDE levels measured in the general population in the United States of America have not been shown to steadily decline over the past decade (Hurley et al., 2017; Ma et al., 2013). The highest mean serum concentration was observed for congener BDE47 in older American adults in the 2005-2006 NHANES pooled serum samples, at 61.4 ng/g lipids (Sjödin et al., 2014). Some authors have identified occupational groups that could be more exposed to PBDEs than the general population, such as underground parking employees, firefighters, carpet installers, foam recyclers and electronic waste recyclers (Alexander and Baxter, 2016; Julander et al., 2005; Li et al., 2016; Park et al., 2015; Stapleton et al., 2008; Zheng et al., 2014).

In adults, PBDEs are suspected to be associated with various health effects generally related to their endocrine disrupting properties. Congener BDE153 has been found to be associated with a lower sperm count (Akutsu et al., 2008), BDE47, 99 and 100 to lower follicule-stimulating hormone (FSH) and luteinizing hormone (LH) levels (Meeker et al., 2009), and BDE99 and 100 to an increased prevalence of hypothyroidism in women (Oulhote et al., 2016). A study in American office workers has also showed that a serum increase in BDE47 was associated with a thyroxin (T4) decrease (Makey et al., 2016).

Despite the increasing evidence that PBDEs are harmful substances to which some workers can be highly exposed, there are no regulatory occupational exposure limits. In order to provide some occupational comparative measures, the present study aims to determine PBDE levels in the general American and Canadian adult working populations using national survey data, and to identify industries and occupational groups with higher exposure to certain PBDE congeners.

3.3. Materials and methods

3.3.1. Study participants

Data came from two recurrent national population cross-sectional surveys, the National Health And Nutrition Examination Survey (NHANES), established by the U.S. Center for Disease Control and Prevention in 1999, and the Canadian Health Measures Survey (CHMS), launched in 2007 and carried out by Statistics Canada (Statistics Canada, 2011; Zipf et al., 2013). Each survey cycle includes household interviews, a standardized physical examination, a medical history and the collection of biological specimens. In the 2003-2004 NHANES cycle, a subsample of 2040 individuals aged 16 years and older were randomly selected for measurement of serum levels of PBDE congeners. In the 2007-2009 CHMS data collection (cycle 1), PBDEs were measured in the plasma of a selected subsample of 1696 participants aged 20 years and older. Our analysis was restricted to participants aged 20 to 65 years old, more susceptible to be working, in each survey.

Among data available in both surveys, some sociodemographic variables are thought or known to be associated with exposure to PBDEs. Included in the present analysis are age, sex, education, race/ethnicity, body mass index (BMI) and cigarette smoking. To comply with Statistics Canada data suppression rules, only results with an unweighted number of more than 30 subjects can be presented for CHMS. Consequently, due to small sample size (n<30) for ethnic groups other than “White” in the CHMS PBDE sub-sample, we had to dichotomize ethnic background for both surveys into “European descent” and “Other and multi-ethnic”. The latter comprises “Mexican American”, “Other Hispanic”, “Non-Hispanic Black” and “Other Race - Including Multi-Racial” for NHANES, and “Chinese”, “South Asian, Black, Filipino”, “Latin American”, “Southeast Asian”, “Arab”, “West Asian”, “Japanese” and “Korean” for CHMS. “European descent” is characterized as “Non-Hispanic White” in NHANES and “White” in CHMS. Cigarette smoking was defined as a positive answer to the question “Have you smoked at least 100 cigarettes in your entire life? / In your lifetime, have you smoked a total of 100 or more cigarettes (about 4 packs)?” in both surveys. Working status was determined to be either “working with a job or company right now” or “employed but not working at the moment” for NHANES, and as “working with a job or company last week", "working with a job or company at some point in the past 12 months" or "working with a job or company from which you were absent last week" for CHMS.

3.3.2. Serum/plasma PBDEs

Fasting serum samples were collected at a Mobile Examination Center, then frozen and shipped to the Division of Environmental Health Laboratory Sciences (National Center for Environmental Health, CDC) for NHANES. For CHMS, fasting plasma samples were collected and handled similarly before being sent to the Centre de toxicologie du Québec (CTQ) of the Institut national de santé publique du Québec (INSPQ). Laboratory methods for congener measurement are described in each survey's laboratory procedure manuals (Center for Disease Control and Prevention, 2007; Health Canada, 2010). Briefly, they both utilized solid-phase extraction, followed by sample cleanup and gas chromatography coupled to mass spectrometry (MS), where NHANES used isotope dilution high-resolution MS (Sjödin et al., 2004) and CHMS used a gas chromatograph coupled to an electron capture detector and MS (Health Canada, 2010). The limits of detection for all congeners are presented in Table 3.1. The mean coefficient of variation for the method in NHANES is published and lies between 5% and 18% for all PBDE congeners (Center for Disease Control and Prevention, 2007), but the CVs are not published for the method employed in CHMS (Haines et al., 2017).

PBDEs are lipid soluble and their concentration is therefore dependant on the serum lipid content. Total lipids were calculated as the sum of triglycerides and total cholesterol. Lipids were analyzed enzymatically at the Lipid Laboratory of Johns Hopkins University School of Medicine for NHANES, and at the Nutrition Research Division at the Health Canada laboratories for CHMS (Center for Disease Control and Prevention, 2006; Health Canada, 2010).

Table 3.1. Polybrominated flame retardants analyzed in NHANES and CHMS, limits of detection, geometric mean lipid adjusted serum/plasma LODs and percentage of censored data for workers and non-workers.

		NHANES				CHMS			
				%<LOD				%<LOD	
Name of congener	**Abbrev.**	**LOD (pg/ml)**	**Geometric mean LOD (ng/g lipids)**	**Non-Workers** (n=360)	**Workers** (n=780)	**LOD (pg/ml)**	**Geometric mean LOD (ng/g lipids)**	**Non-Workers** (n=217)	**Workers** (n=1120)
2,2',4,4',5,5'-hexabromobiphenyl	PBB153	2.5	0.48	16.6	14.3	20.0	3.27	(97.3)[a]	
4,4'-dibromodiphenyl ether	BDE15	-	-	-	-	30.0	4.89	100	100
2,2',4-tribromodiphenyl ether	BDE17	2.5	0.42	94.5	95.9	30.0	4.89	100	100
2,3',4-Tribromodiphenyl ether	BDE25	-	-	-	-	30.0	4.89	100	100
2,4,4'-tribromodiphenyl ether	BDE28	2.5	0.46	22.0	17.8	30.0	4.91	(97.4)[a]	
2',3,4-Tribromodiphenyl ether	BDE33	-	-	-	-	30.0	5.15	100	100
2,2',4,4'-tetrabromodiphenyl ether	BDE47	6.2	2.49	4.6	1.4	30.0	5.14	30.7	22.7
2,3',4,4'-tetrabromodiphenyl ether	BDE66	2.8	0.43	72.9	80.6	-	-	-	-
2,2',3,4,4'-pentabromodiphenyl ether	BDE85	16.4	1.02	72.8	78.5	-	-	-	-
2,2',4,4',5-pentabromodiphenyl ether	BDE99	7.0	2.56	30.0	33.6	20.0	3.31	71.6	73.9
2,2',4,4',6-pentabromodiphenyl ether	BDE100	2.5	0.81	7.8	4.9	20.0	3.32	75.8	72.9
2,2',4,4',5,5'-hexabromodiphenyl ether	BDE153	17.0	1.18	6.3	6.2	20.0	3.33	66.5	55.9
2,2',4,4',5,6'-hexabromodiphenyl ether	BDE154	2.5	0.45	42.8	46.3	-	-	-	-
2,2',3,4,4',5',6-heptabromodiphenyl ether	BDE183	4.1	0.76	80.6	83.1	-	-	-	-

LOD: limit of detection
"-" denotes a congener that is not measured
[a] Due to n<30 in both categories, it was not possible to show stratified results and this percentage represents the total sample.

3.3.3. Industry categories

In NHANES 2003-2004 cycle, industry was classified into 45 categories according to the U.S. Census Bureau's Census 2000 Indexes of Industry and Occupations (derived from the 2002 North American Industry Classification System [NAICS]), whereas CHMS cycle 1 used the 2002 North American Industry Classification System (NAICS) for a classification of industry into 20 categories. These classifications are comparable to the International Standard Industrial Classification (ISIC) revision 3.1. In order to get groups of larger size, we aggregated industry categories into 10 groups according to potential exposure to flame retardants. Groupings are based on a literature research and expert opinion from a Canadian Registration Board of Occupational Hygienists certified industrial hygienist, who has extensive field experience in occupational health research; the groups were determined as follows: 1 "Agriculture, forestry, fishing", 2 "Utilities and construction", 3 "Manufacturing: Durable Goods", 4 "Manufacturing: Non-Durable Goods", 5 "Trade, transportation and warehousing", 6 "Information, finance, real estate, education and entertainment", 7 "Professional services", 8 "Health and food services", 9 "Other services", 10 "Public administration and armed forces". A detailed breakdown of the groups can be found in supplementary Table S3.1.

3.3.4. Statistical analyses

Data analyses were performed using SPSS version 24.0 (IBM Corp. Armonk, NY). Both surveys provide weights to account for a complex, multistage, probability sampling design, in order to get regional representativeness in terms of age, sex and race/ethnicity. However, since the goal of this paper is to compare workers of industrial sectors with each other, rather than generalizing to the whole US or Canadian population, weights were not used in our analyses, as weighting could over-adjust for covariables such as age, sex and ethnicity. Weighted population descriptives were nonetheless calculated and can be found in supplementary Table S3.2. There were minimal differences between weighed and unweighted PBDE analyses (data not shown).

The distribution of all congener concentrations was right-skewed and therefore data was natural-log transformed. In NHANES, measurements that were below the LOD were provided as already replaced by their specific LODs divided by the square root of 2, and also already adjusted on individual blood lipid content. In CHMS, measurements that were below the LOD were missing but another variable indicated whether it was below the LOD or not, so that it could be imputed with the provided LODs divided by the square root of 2, and subsequently adjusted on individual blood lipid levels (Hornung and Reed, 1990). The congeners analyzed in NHANES and in CHMS are listed in table 3.1, as well as the limits of detection, the geometric mean LOD for each congener, and the percentage of censored data for workers and non-workers.

Only PBDE congeners where the percentage of censored data was below 75% in both surveys were included in the analyses. Survey-specific descriptive analyses included geometric means (GM) and their 95% confidence interval, geometric standard deviations, medians, and the GMs were also stratified by working status and by sex. Student's t-tests and chi-square tests of independence were utilised to examine differences in PBDE serum or plasma concentrations among groups of different demographic characteristics and among groups of the two different surveys. Simple one-way analyses of variance (ANOVA) were performed to examine significant differences in workers of the different industry groups in each survey. Multivariable regressions included, for each PBDE congener, the log-transformed, lipid-adjusted concentration as the dependant variable, as well as age (continuous), sex (dichotomous), working status (dichotomous), ethnic background (dichotomous), BMI (continuous) and smoking status (dichotomous) as covariates. Subsequently, these regression analyses were stratified on working status to observe the effect of sex among non-workers and workers, adjusted on the other covariates. Pearson correlation coefficients were calculated to assess association between the ln-transformed PBDE congeners.

3.4. Results

Among all of the congeners analyzed, only four were detected in more than 25% of the two survey populations, namely BDE47, BDE99, BDE100 and BDE153. CHMS has reported LODs 7 to 14 times higher than those of NHANES, and consequently has a much higher proportion of values below the LOD for all congeners (Table 3.1).

PBDE levels were measured in 1141 and 1337 participants aged 20-65 years old in NHANES and CHMS, respectively (flowchart of the subject selection in supplementary Figure S1). Population characteristics for both surveys are presented in Table 3.2. There is a significantly higher proportion of non-workers in NHANES (31.6%) than in CHMS (16.2%) ($\chi 2$ (1) = 81.13, p<0.001), and a lower proportion of women among non-workers in NHANES (63.6% for NHANES against 74.2% for CHMS; $\chi 2$ (1) = 6.92, p=0.009). The demographic characteristics differ between the two databases for ethnicity, as NHANES contains a larger proportion of subjects in the "Other and multi-ethnic" category compared to CHMS (52.0% for NHANES against 14.4% for CHMS; $\chi 2$ (1) = 382.7, p<0.001). The differences in ethnicity are reduced when the respective survey weights are applied (supplementary Table S3.3). CHMS subjects are older than NHANES subjects, and workers are significantly younger than non-workers in both surveys (all Student's t-test results with p<0.001).

Geometric means, as well as geometric standard deviations and medians of the four lipid-adjusted congeners for both surveys, stratified by working status, are presented in table 3.3. The GMs of the four congeners are significantly higher in NHANES than in CHMS for all subjects and by work strata (P<0.001). Geometric means and their confidence intervals, stratified by working status and gender, are presented in Table 3.4. In both surveys and for most congeners, there are no major differences in GM levels between workers and non-workers. For the BDE47 congener in CHMS, the GMs are statistically significantly higher in workers, for all subjects together and for women specifically (Tables 3.3 and 4, P<0.03). For BDE153, the GMs are statistically significantly higher in workers only in CHMS (Table 3.3, p=0.005), and men have significantly higher GM levels than women among workers of both surveys (P<0.001).

Table 3.2. Characteristics of the adult (20-65 years old) NHANES and CHMS populations in the PBDE subsample

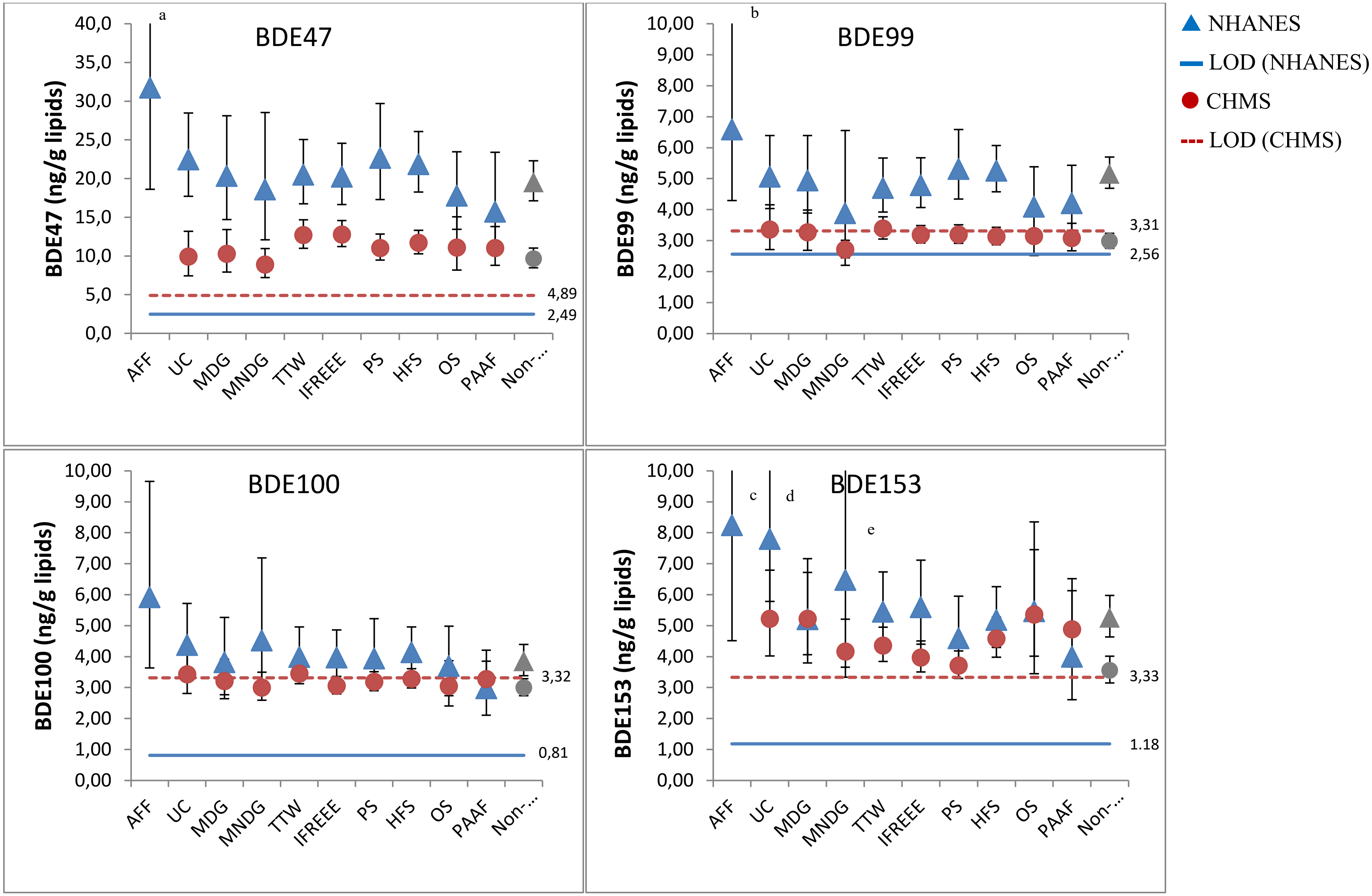
		NHANES			CHMS		
		All (n=1141)	**Non-Workers** (n=360; 31.6%)	**Workers** (n=780; 68.4%)	**All** (n=1337)	**Non-Workers** (n=217; 16.2%)	**Workers** (n=1120; 83.8%)
Age (Mean [95%CI])		40.5 [39.8-41.3]	43.0 [41.5-44.5]	39.4 [38.5-40.2]	43.1 [42.4-43.7]	49.7 [47.9-51.5]	41.8 [41.1-42.5]
Sex	**Men**	534 [46.8]	131 [36.4]	403 [51.7]	620 [46.4%]	56 [25.8%]	564 [50.4%]
(N [%])	**Women**	607 [53.2]	229 [63.6]	377 [48.3]	717 [53.6%]	161 [74.2%]	556 [49.6%]
Education	**No high school diploma**	279 [24.5]	134 [37.2]	145 [18.6]	176 [13.2]	52 [24.0]	124 [11.1]
(N [%])	**High school graduate**	861 [75.5]	226 [62. 8]	634 [81.4]	1152 [86.2]	164 [75.6]	988 [88.2]
Ethnicity	**European descent**	548 [48.0]	156 [43.3]	392 [50.3]	1105 [82.7]	168 [77.4]	937 [83.7]
(N [%])	**Other and multi-ethnic**	593 [52.0]	204 [56.7]	388 [49.7]	193 [14.4]	39 [18.0]	154 [13.8]
BMI	**≤30 kg/m^2**	732 [65.1]	223 [61.9]	509 [65.3]	1014 [75.8]	155 [71.4]	859 [76.7]
(N [%])	**>30 kg/m^2**	392 [34.9]	128 [35.6]	263 [33.7]	323 [24.2]	62 [28.6]	261 [23.3]
Smoking status	**Smoker**	556 [48.7]	196 [54.4]	359 [46.0]	678 [50.7]	119 [54.8]	559 [49.9]
(N [%])	**Non-smoker**	583 [51.1]	162 [45.0]	421 [54.0]	659 [49.3]	98 [45.2]	561 [50.1]

BMI: body mass index calculated as [weight in kilograms/(height in meters)^2]

Working status was not a significant predictor of PBDE levels in multivariable regressions adjusted for age, sex, BMI, smoking status, ethnicity and education, in both surveys. However, considering the percent change in PBDE levels between men and women by working status (Table 3.5), sex is a more important predictor of exposure to BDE153 among workers than among non-workers in NHANES (33.4% in workers, 24.5% in non-workers) and in CHMS (18.8% in workers, 5.4% in non-workers). In multivariable regressions, women had a significantly lower level of BDE153 in both surveys.

Figure 1 shows the lipid-adjusted geometric means and 95% confidence intervals for workers in the 10 industrial groupings, for both surveys (except for Agriculture, forestry and fishing in CHMS where $n<30$), as well as their respective average LOD value. NHANES geometric means are significantly higher than CHMS ones in most industrial groups for congeners BDE47 and BDE99, although not different from levels in non-workers. In CHMS, workers in the Information, finance, real estate, education and entertainment (IFREE) and in the Trade, transportation and warehousing (TTW) groups have a significantly higher level of BDE47 than non-workers (IFREE $P=0.003$, TTW $P=0.006$).

Pearson correlation coefficients (Table S3.3) showed moderate to strong significant associations ($p<0.01$) of the four congeners with each other in both surveys, but they were generally weaker in CHMS (0.45 to 0.84) than in NHANES (0.56 to 0.94). BDE47 showed the strongest correlation with BDE100 ($r = 0.94$) in NHANES, and BDE99 with BDE100 ($r=0.84$) in CHMS.



a
BDE47
BDE47 (ng/g lipids)
40,0
35,0
30,0
25,0
20,0
15,0
10,0
5,0
0,0
4,89
2,49
AFF
UC
MDG
MNDG
TTW
IFREEE
PS
HFS
OS
PAAF
Non-...
b
BDE99
BDE99 (ng/g lipids)
10,00
9,00
8,00
7,00
6,00
5,00
4,00
3,00
2,00
1,00
0,00
3,31
2,56
NHANES
LOD (NHANES)
CHMS
LOD (CHMS)
BDE100
BDE100 (ng/g lipids)
3,32
0,81
c
d
e
BDE153
BDE153 (ng/g lipids)
3,33
1.18

Figure 3.1. Geometric means (ng/g lipids) and 95% confidence intervals of serum/plasma 2,2',4,4'-tetrabromophenyl ether (BDE47), 2,2',4,4',5-pentabromophenyl ether (BDE99), 2,2',4,4',6-pentabromodiphenyl ether (BDE100) and 2,2',4,4',5,5'-hexabromophenyl ether (BDE153), for NHANES (▲) and CHMS (●), for 10 industrial groups: Agriculture, forestry, fishing (AFF), Utilities and construction (UC), Manufacturing Durable Goods (MDG), Manufacturing Non-Durable Goods (MNDG), Trade, transportation and warehousing (TTW), Information, finance, real estate, education and entertainment (IFREEE), Professional services (PS), Health and food services (HFS), Other services (OS), Public administration and armed forces (PAAF), Non-workers (Non-workers). Geometric mean value for LOD (ng/g lipids) are depicted by a blue line for NHANES and a red dashed line for CHMS. Upper confidence intervals outside the scale of the axis: [a]54.2; [b]12.8; [c]15.1; [d]10.5; [e]11.5.

Table 3.3. Geometric means and their 95% confidence intervals, geometric standard deviations and medians of serum/plasma PBDE concentrations (ng/g lipid) in the PBDE subsample of NHANES and CHMS (20-65 year-old)

	NHANES									CHMS								
	All (n=1141)			Non-Workers (n=360)			Workers (n=780)			All (n=1337)			Non-Workers (n=217)			Workers (n=1120)		
	GM [95%CI]	GSD	Md	GM [95%CI]	GSD	Md	GM [95%CI]	GSD	Md	GM [95%CI]	GSD	Md	GM [95%CI]	GSD	Md	GM [95%CI]	GSD	Md
BDE47	20.5 [19.1, 21.9]	3.1	19.3	19.5 [17.1, 22.3]	3.4	19.3	20.9 [19.3, 22.7]	3.0	19.4	11.1 [10.6, 11.7]	2.7	10.1	9.7 [8.5, 11.0]	2.6	10.4	11.4* [10.8, 12.1]	2.7	9.1
BDE99	5.0 [4.7, 5.3]	2.9	4.1	5.2 [4.6, 5.8]	3.0	4.2	4.9 [4.5, 5.3]	2.9	4.1	3.2[a]	1.9	2.6	3.0[a]	1.8	2.6	3.2[a]	2.0	2.5
BDE100	4.0 [3.7, 4.3]	3.2	3.5	3.8 [3.4, 4.4]	3.4	3.3	4.0 [3.7, 4.4]	3.1	3.6	3.2[a]	2.0	2.6	3.0[a]	2.0	2.6	3.2[a]	2.0	2.4
BDE153	5.4 [5.0, 5.8]	3.3	4.7	5.3 [4.6, 6.0]	3.3	4.6	5.5 [5.0, 6.0]	3.3	4.7	4.2 [4.0, 4.4]	2.6	2.9	3.6 [3.2, 4.0]	2.4	3.0	4.4** [4.1, 4.6]	2.6	2.5

GM: Geometric mean; GSD : Geometric standard deviation of the mean; Md : median

[a] Due to proportion of censored data above 70%, confidence intervals were considered meaningless.

* P = 0.029 between workers and non-workers, Student's t-test

** P = 0.005 between workers and non-workers, Student's t-test

Table 3.4. Lipid adjusted geometric means and 95% confidence intervals of serum or plasma PBDE concentrations, in the PBDE subsample (20-65 year-old), stratified by sex and working status.

			NHANES			**CHMS**		
			All (n=1141)	**Non-Workers** (n=360)	**Workers** (n=780)	**All** (n=1337)	**Non-Workers** (n=217)	**Workers** (n=1120)
Geometric mean [95%CI] (ng/g lipid)	**BDE47**	Men	20.9 [18.9, 23.2]	20.7 [16.2, 26.6]	21.0 [18.8, 23.4]	11.2 [10.4, 12.2]	10.7 [8.0, 14.4]	11.3 [10.4, 12.3]
		Women	20.0 [18.2, 22.0]	18.9 [16.2, 22.0]	20.8 [18.5, 23.5]	11.1 [10.3, 11.9]	9.3 [8.1, 10.8]	11.6 [10.7, 12.6]*
	BDE99	Men	5.2 [4.7, 5.7]	5.7 [4.5, 7.2]	5.0 [4.5, 5.6]	3.2[a]	3.4[a]	3.2[a]
		Women	4.8 [4.4, 5.3]	4.9 [4.3, 5.6]	4.8 [4.2, 5.4]	3.1[a]	2.8[a]	3.2[a]
	BDE100	Men	4.1 [3.7, 4.6]	4.3 [3.4, 5.5]	4.1 [3.6, 4.5]	3.2[a]	3.3[a]	3.2[a]
		Women	3.9 [3.5, 4.2]	3.6 [3.1, 4.2]	4.0 [3.5, 4.6]	3.2[a]	2.9[a]	3.3[a]
	BDE153	Men	6.6 [5.9, 7.3]	7.1 [5.6, 8.9]	6.4 [5.7, 7.3]	4.7 [4.3, 5.1]	3.7 [2.9, 4.7]	4.8 [4.4, 5.2]
		Women	4.6 [4.1, 5.0]**	4.4 [3.8, 5.2]**	4.6 [4.1, 5.3]**	3.8 [3.6, 4.1]**	3.5 [3.3, 4.0]	4.0 [3.7, 4.3]**

[a] Due to proportion of censored data above 70%, confidence intervals were considered meaningless.
* P=0.013 between workers and non-workers, Student's t-test
** P<0.001 between men and women, Student's t-test

Table 3.5. Adjusted[a] percent change (95% confidence interval) in serum/plasma PBDE congeners concentration in ng/g lipids, associated with sex[b].

	NHANES			CHMS		
	All (n=1141)	**Non-Workers** (n=360)	**Workers** (n=780)	**All** (n=1337)	**Non-Workers** (n=217)	**Workers** (n=1120)
BDE47	-3.8 [-16.6, 11.0]	-0.3 [-15.5, 43.3]	-12.5 [-34.2, 16.3]	3.2 [-7.7, 15.3]	-6.2 [-31.2, 27.9]	5.1 [-6.7, 43.6]
BDE99	-7.4 [-19.4, 6.2]	-3.0 [-17.6, 14.2]	-15.9 [-35.1, 9.09]	-1.0 [-8.1, 6.7]	-16.1 [-30.8, 1.8]	1.5 [-6.4, 10.2]
BDE100	-5.5 [-18.4, 9.3]	-0.2 [-15.8, 18.4]	-16.3 [-37.0, 11.2]	1.8 [-5.8, 9.9]	-10.0 [-27.6, 11.9]	3.6 [-4.6, 12.6]
BDE153	-27.9 [-37.8, -16.4]*	-24.5 [-36.8, -9.8]*	-33.4 [-49.0, -12.9]*	-16.8 [-25.1, -7.6] *	-5.4 [-28.8, 25.7]	-18.8 [-27.5, -8.9] *

[a] Adjusted for age, BMI, smoking status, ethnicity and education
[b] Male is the reference group
* P < 0.05

3.5. Discussion

NHANES and CHMS are national surveys that provide biological measures of PBDE congeners for a representative sample of their respective populations. Focus on variables that are not considered in the sampling design (e.g. working status) may explain why the PBDE subsample contains a larger proportion of non-workers than what is observed in the national populations, even after applying sampling weights. This can also be attributable to the lower availability of workers to participate in such time-consuming surveys. A background exposure to PBDEs could be detected in both surveys, but with levels that varied greatly between congeners and between surveys. Although CHMS concentrations of BDE47 are twice as low as those in NHANES, the medians reported here for both surveys (Table 3.3) are still much higher than medians calculated in comparable studies from other countries like Sweden (BDE47 = 0.49 ng/g lipids; 2010-2011), France (BDE47 = 1.56 ng/g lipids; 2003-2005), Germany (BDE47 = 0.38 ng/g lipids; 2013), or Australia (BDE47 = 3.96 ng/g lipids; 2008-2011) (Bjermo et al., 2017; Brasseur et al., 2014; Fromme et al., 2015; Stasinska et al., 2014). Only two NHANES participants have levels above the biomonitoring equivalent reference dose of 520 ng/g lipids (Krishnan et al., 2011) proposed by the United States Environmental Protection Agency and Health Canada for BDE99. The high concentrations of BDE47, as well as the strong correlations between BDE47, 99 and 100, are consistent with the widespread use of the technical mixture PentaBDE in North-America (de Wit, 2002; Rawn et al., 2014; Vonderheide et al., 2008). While some authors have noticed a temporal decline in serum concentration of certain PBDE congeners in the past couple of years in America (Sjödin et al., 2014), others have reported an initial decline but a resurgence more recently (Hurley et al., 2017; Ma et al., 2013). This may suggest that the levels measured in both surveys are a fair representation of the current background exposure level, even if the two survey cycles used here were held a decade ago (Trudel et al., 2011).

There were no consistent differences PBDE when comparing workers and non-workers, in both surveys. Workers generally don’t have higher geometric mean PBDE levels than non-workers except for congeners BDE47 and BDE153 in CHMS, and very few industries stand out from the others. This may indicate that environmental exposure to these PBDE congeners is widespread in the United States and Canada to the extent that it blurs differences in occupational exposures. However, if both surveys had been able to analyze BDE209 at the time, a different conclusion might have been reached, as this congener has been reported in high concentrations in various occupational settings (Sjödin et al., 2001; Wang et al., 2010). The ratios between the industry with the highest geometric mean and the one with the lowest vary between 1.7 and 2.0 among congeners in NHANES and between 1.1 and 1.4 among congeners in CHMS. BDE47 and 99 levels differed significantly by industry group between the two surveys: this may indicate either country-specific industrial group differences in exposure to flame retardants, or differences in working population characteristics within the industrial groups between these two countries. Higher concentrations of BDE47 and 99 are indeed reported in several media that could be sources of human intake, such as fish and meat, or air and dust (Roosens et al., 2009). Workers in the IFREE industry group can arguably be highly exposed to electronics and foam from upholstery in cars, both known to contain pentaBDE, which could explain their higher BDE47 levels in CHMS (Li et al., 2016).

There are significant sex differences in BDE153 serum levels in both surveys, which are even more pronounced in workers. Sex differences have also been observed in a Swedish population study, but not in a similar German study (Bjermo et al., 2017; Fromme et al., 2015). An in vivo toxicology study on rodents also found a small but significant difference in the fatty tissue distribution of BDE153 between male and female rats, which was however deemed biologically insignificant by the authors (Sanders et al., 2006). The larger differences in percent change for this congener in workers may be partly explained by higher occupational exposures to flame retardants in jobs traditionally held by men, such as firefighting and carpet installers (Park et al., 2015; Stapleton et al., 2008). But this still wouldn't explain entirely why these differences are only observed for this specific congener, as it is found in conjunction with other congeners in commercial formulations.

One of the limitations of this study is related to the size of the PBDE sub-sample in both surveys, which impedes a finer analysis of the industrial groups, even with the 10 broader groupings used here; thus, it was not possible to isolate industries with expected higher exposures, such as electronic recycling or polyurethane carpet installation, using these data sources. Moreover, depending on the coding criteria used, some of these highly exposed industries can be classified into different industrial groups (e.g. electronics recycling can be classified in Trade, transportation and warehousing as well as in Professional services), thereby introducing a classification bias that decreases the possibility of highlighting differences in exposures. Moreover, a high proportion of censored data, especially in CHMS, necessitates more imputation of missing values which increases type 1 error, artificially reduces the variability of estimates and may under- or over-estimate the calculated results. Other imputation approaches could yield different results (Hewett and Ganser, 2007; Huynh et al., 2016), but to facilitate comparison with previously published papers on PBDE exposure in national surveys, imputation with LOD/√2 was deemed appropriate, despite its limitations. Methodological differences in sample detection between the laboratories employed for these two surveys are thought to explain their considerably different LODs. Nonetheless, the levels actually detected in NHANES and CHMS can still indicate a population exposure that is much higher than that of similar non-North American populations.

This study succeeded in bringing out a background exposure level of PBDE in adult workers through the analysis of population exposure surveys. Moreover, the fact that certain observations in one country were corroborated in the other increases our confidence in the robustness of the results.

3.6. Conclusion

The results of this analysis show that exposure to PBDEs in a sample of the North American population is fairly high, compared to other countries. Moreover, working status as defined in these surveys doesn't seem to significantly influence exposure, as opposed to sex with congener BDE153 specifically. Using industry codes as a proxy of exposure did not provide sufficient sensitivity to shed light on significantly exposed worker groups. These results can be used as a comparative background exposure level in the analysis of occupational exposure to PBDEs.

3.7. Acknowledgments

Acknowledgments are in order for the much appreciated help from Brigitte Roberge in coding the industries. Thank you also to the CTQ lab staff who could provide more information on the CHMS chemical analysis. The corresponding author received an entrance scholarship from the Quebec inter-University Centre for Social Statistics (QICSS).

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3.9. Appendix

Figure S3.1. Flowchart illustrating subject selection

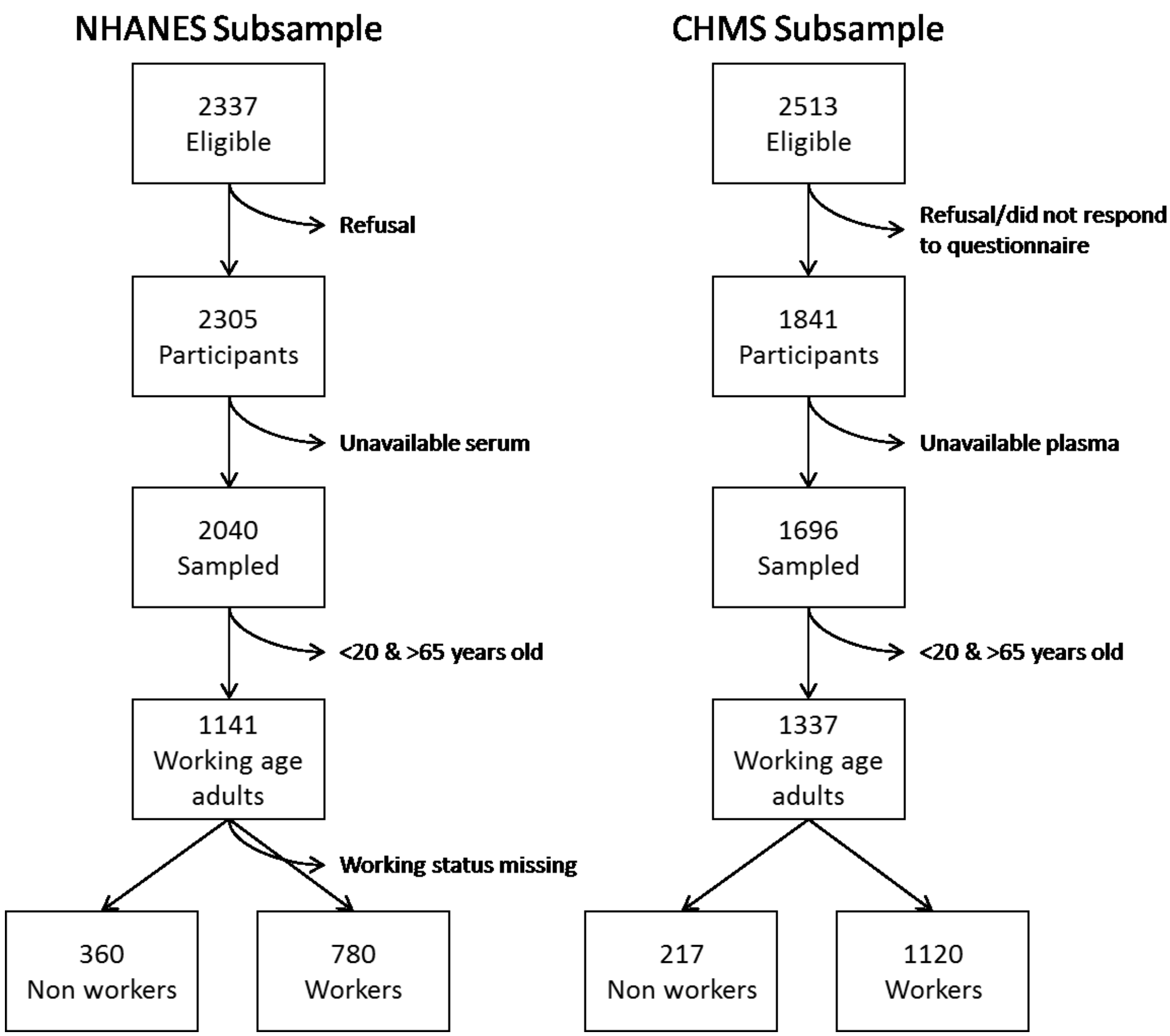

Table S3.1. Correspondence between the 10 combined industry categories used in this study and the categories used in NHANES (2003-2004) and CHMS (Cycle 1).

	Combined categories	NHANES categories (2003-2004)	CHMS categories (Cycle 1)
1	Agriculture, forestry, fishing	Agriculture production Agricultural services, forestry, and fishing	Agriculture, Forestry, Fishing
2	Utilities and construction	Utilities Construction	Utilities Construction
3	Manufacturing: Durable Goods	Mining Mfg.-Lumber and wood products, including furniture Mfg.-Metal industries Mfg.-Machinery, except electrical Mfg.-Electrical machinery, equipment, and supplies Mfg.-Transportation equipment Mfg.-Miscellaneous and not specified manufacturing industries	Mining Manufacturing: Durable Goods
4	Manufacturing: Non-Durable Goods	Mfg.-Food and kindred products Mfg.-Textile mill products Mfg.-Apparel and other finished textile products Mfg.-Paper products, printing, publishing, and allied industries Mfg.-Chemicals, petroleum, and coal products Mfg.-Rubber, plastics, and leather products	Manufacturing: Non-Durable Goods
5	Trade, transportation and warehousing	Wholesale Trade, Durable goods Wholesale Trade, Non-durable and not specified goods Retail-Department stores Retail-Food stores Retail-Vehicle dealers, supply and service stores Retail-Apparel and accessory stores Other Retail trade Trucking service Transportation, except trucking	Wholesale Trade Retail Trade Transportation, Warehousing
6	Information, finance, real estate, education and entertainment	Communications Banking and other finance Insurance and real estate Educational services Entertainment and recreation services	Information Services Finance, Insurance Real Estate, Rental, Leasing Education Service Arts, Entertainment, Recreation
7	Professional services	Other professional and related services Business services	Professional, Scientific, Technical Services Management, Administrative, Waste Services

	Combined categories	NHANES categories (2003-2004)	CHMS categories (Cycle 1)
8	Health and food services	Offices of health practitioners Hospitals Health services, n. e. c. Social services Retail-Eating and drinking places Lodging places	Health Care, Social Assistance Accommodation, Food Services
9	Other services	Repair services Personal services, except private households and lodging Private households	Other Services Private Household
10	Public administration and armed forces	Justice, public order, and safety Public administration, except justice, public order, safety Military & national security	Public Administration Armed Forces
	Missing	Blank but applicable	Text present but uncodable Blank but applicable

Table S3.2. Weighted characteristics of the adult NHANES and CHMS populations (20-65 years old) in the PBDE subsample

		NHANES			CHMS		
		All	**Non-Workers** 25.0%	**Workers** 75.0%	**All**	**Non-Workers** 13.2%	**Workers** 86,8%
Age (Mean)		40,9	43,59	40,0	41,5	49	40,4
Sex (%)	**Men**	48,8	37,1	52,8	49,1	17,7	53,9
	Women	51,2	62,9	47,2	50,9	82,3	46,1
Education (%)	**No high school diploma**	15,6	27,1	11,8	13,5	26,9	11,5
	High school graduate	84,4	72,9	88,2	86,5	73,1	88,5
Ethnicity (%)	**European descent**	69,7	64,6	71,5	82,7	76,7	83,6
	Other and multi-ethnic	30,3	35,4	28,5	17,3	23,3	16,4
BMI (%)	**$\leq$30 kg/m^2**	64,9	64,7	64,9	78,5	73,9	79,1
	>30 kg/m^2	34,0	33,9	34,0	21,5	26,1	20,9
Smoking status (%)	**Smoker**	49,1	39,9	52,2	46,5	48,4	46,2
	Non-smoker	50,8	59,8	47,8	53,5	51,6	53,8

Table S3.3. Pearson correlation* coefficients between lipid-adjusted serum/plasma PBDE levels among workers and non-workers.

	NHANES						CHMS					
	BDE99		**BDE100**		**BDE153**		**BDE99**		**BDE100**		**BDE153**	
	Workers	Non-Workers	Workers	Non-Workers	Workers	Non-Workers	Workers	Non-Workers	Workers	Non-Workers	Workers	Non-Workers
BDE47	.905	.906	.923	.938	.596	.622	.795	.773	.778	.703	.445	.489
BDE99			.844	.871	.561	.582			.842	.732	.449	.426
BDE100					.772	.770					.668	.763

* P< 0.01 (2-tailed) for all coefficients.

Chapitre 4. Assessment of occupational exposure to organic flame retardants: a systematic review.

Assessment of occupational exposure to organic flame retardants: a systematic review

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Cet article répond au second objectif de cette thèse, c'est-à-dire celui d'identifier les milieux de travail où l'exposition aux ignifuges est la plus importante. Dans le cadre de cette revue systématique, les carences et les failles des études compilées sont également relevées afin d'y formuler des recommandations sur la tenue d'études sur l'évaluation de l'exposition professionnelle aux ignifuges.

L'étudiante a procédé à la collecte de données bibliographiques, et la sélection des articles à inclure a été effectuée en parallèle avec un co-auteur (FL). Le manuscrit a été rédigé par l'étudiante, avec les apports des deux coauteurs, de même qu'à sa révision jusqu'à sa publication. Le manuscrit a été révisé et approuvé par tous les coauteurs.

L'article est publié dans la revue Annals of Work Exposures and Health, qui a un facteur d'impact 2018 de 1.71. PMID: 30852590 DOI: 10.1093/annweh/wxz012

4.1. Abstract

Background

Flame retardants are widespread in common goods, and workers in some industries can be exposed to high concentrations. Numerous studies describe occupational exposure to flame retardants, but the diversity of methods and of reported results renders their interpretation difficult for researchers, occupational hygienists and decision-makers.

Objectives

The objectives of this paper are to compile and summarize the scientific knowledge on occupational exposure to flame retardants, as well as to identify research gaps and to formulate recommendations.

Methods

Five databases were consulted for this systematic literature review (Embase, Medline [Pubmed], Global health, Web of Science and Google Scholar), with terms related to occupational exposure and to flame retardants. Selected studies report quantitative measurements of exposure to organic flame retardants in a workplace, either in air, dust, or in workers' biological fluids. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement guidelines were followed.

Findings

The search yielded 1540 published articles, of which 58 were retained. The most frequently sampled flame retardants were polybrominated diphenyl ethers and novel brominated flame retardants. Offices and electronic waste recycling facilities were the most studied occupational settings, and the highest reported exposures were found in the latter, as well as in manufacturing of printed circuit boards, in aircrafts and in firefighters. There were recurrent methodological issues, such as unstandardized and ill-described air and dust sampling, as well as deficient statistical analyses.

Conclusions

This review offers several recommendations. Workplaces such as e-waste recycling or manufacturing of electronics, as well as firefighters and aircraft personnel should be granted more attention from researchers and industrial hygienists. Methodical and standardized occupational exposure assessment approaches should be employed, and data analysis and reporting should be more systematic. Finally, more research is needed on newer chemical classes of flame retardants, on occupational exposure pathways, and on airborne flame retardant particle distribution.

Keywords : Flame Retardants, Brominated Diphenyl Ethers, Occupational Exposure, Electronic Waste Recycling, Firefighters, Systematic review, Sampling methods

4.2. Introduction

Organic flame retardants are chemicals used to slow down or prevent the burning process of fabrics, plastics and other materials to which they are added (Dishaw et al. 2014). Various flame retardants (FRs) have been introduced in consumer goods at an increasing pace since the mid twentieth century to meet fire safety standards. A non-negligible background exposure level can be detected in the serum and urine of the general population (Brasseur et al. 2014; Butt et al. 2014; Fromme et al. 2015; Gravel et al. 2018). Among the organic compounds introduced since the 1970s, polybrominated diphenyl ethers (PBDEs) have been shown to bioaccumulate and to present endocrine activity; consequently, some commercial formulations were banned and gradually removed from the market (Besis and Samara 2012; Cowell et al. 2017). PBDEs have been superseded by novel brominated FRs (NBFRs), such as hexabromobenzene (HBB) and tetrabromobisphenol A (TBBPA) (Covaci et al. 2011), and more recently by polychlorinated (Dechlorane plus) and various organophosphate (OPs) compounds, such as tris (1-chloro-2-propyl) phosphate (TDCiPP) and triphenyl phosphate (TPhP) (Hoffman et al. 2017a; Tao et al. 2016). Despite the ban of specific formulations of FRs and the withdrawal of some commercial mixtures, those substances may still be found in common goods and can, for years on, off-gas or detach from the materials, adsorb to dust, and therefore be released in the environment (Liagkouridis et al. 2014; Takigami et al. 2008; Webster et al. 2009). Some of the novel formulations, albeit less bioaccumulative, are also suspected to have endocrine active properties or to induce oxidative stress in living organisms (Hill et al. 2018; Hoffman et al. 2017b; Preston et al. 2017; Wu et al. 2012).

As for many contaminants, occupational exposure to FRs can be much higher than environmental exposure (Semple 2005). Indeed, some of the highest concentrations in dust were measured in occupational settings such as offices, aircrafts and electronic waste (e-waste) recycling facilities, as opposed to levels found in house dust (Deng et al. 2014; Dodson et al. 2012; Li et al. 2015; Strid et al. 2014). To date, most evidence on health effects of FRs and risk assessments has been gathered on children, or in animal and in vitro studies (He et al. 2011; Lyche et al. 2015). As the dose-response evidence on adverse effects in exposed adults is still scarce, no occupational exposure limit values (OELs) have been proposed.

As more and more researchers, industrial hygienists and occupational physicians are striving to assess exposure to FRs in several environments and workplaces, our understanding of the actual importance of these compounds is contingent on thorough and reproducible exposure measurements. A small number of reviews on exposure to FRs in various environments have been published, but they focused on home or environmental exposure (Besis and Samara 2012; Coelho et al. 2014; Frederiksen et al. 2009; Mercier et al. 2011; Ni et al. 2013; Sverko et al. 2011; Yu et al. 2016). The objectives of this systematic review are to compile and lay a critical eye on published quantitative assessments of occupational exposure to organic flame retardants in dust, air or biological fluids, in order to report the concentrations found in various formal workplaces and to identify exposure assessment gaps that would benefit from improvement.

4.3. Methods

This systematic review follows the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement guidelines (Moher et al. 2009). The PRISMA checklist for this systematic review is provided in Supplementary Table 4.1.

4.3.1. Search strategy description

Five databases were searched for papers published from database inception until July 2018: Embase, Medline (PubMed), Global Health, Web Of Science and Google Scholar (Bramer et al. 2017). The detailed search strategy is described in Supplementary Table 4.2. The broad search terms "occupational exposure" and "flame retardants" were used, and restricted to studies on Humans. The search in Google Scholar produced more than 15,000 results, of which 1000 were consulted for identification of additional relevant publications. There were no restrictions of language or publication date. A consultation of the reference list of other review papers was also performed.

4.3.2. Inclusion and exclusion criteria

To be included in the review, a study had to report a quantitative assessment of occupational exposure to an organic FR, or an epidemiological study that included at least one group of workers and presented a quantitative exposure assessment to FRs. Based on recommendations for industrial hygiene assessments, sampling media included were air (personal or stationary active sampling), dust (collected by either surface wipe sampling or vacuuming), blood (serum or plasma), and urine (American Industrial Hygiene Association 2015). In order to allow comparison of exposure measurement data to OELs, the American Industrial Hygienists Association (AIHA) recommends that at least six measurements per similar exposure group or task be taken in a given workplace (Waters et al. 2015). However, as very few studies in this review would have met this criterion, the number of required measurements for inclusion was set to at least three measurements per sampling medium (air, dust, blood or urine sample) per workplace in a given study, which still allows for some interpretation of levels of exposure, keeping in mind that the variability could be quite substantial. In the occurrence of a sample size smaller than three per workplace, a study with a total sample size of six per industrial group was deemed acceptable. Where the number of samples was not reported or if it was unclear whether the workplace was in a formal sector, the authors of the paper were contacted.

We excluded studies on children's exposure or on population living in the vicinity of contaminated sites, assessments in informal workplaces (such as in Leung et al. (2011), where makeshift workshops are part of the workers' dwellings), case studies, ecological studies, studies that focused only on household exposure, toxicokinetics research, reviews, letters to the editor and conference abstracts. Individual studies were not assessed for risk of exposure bias.

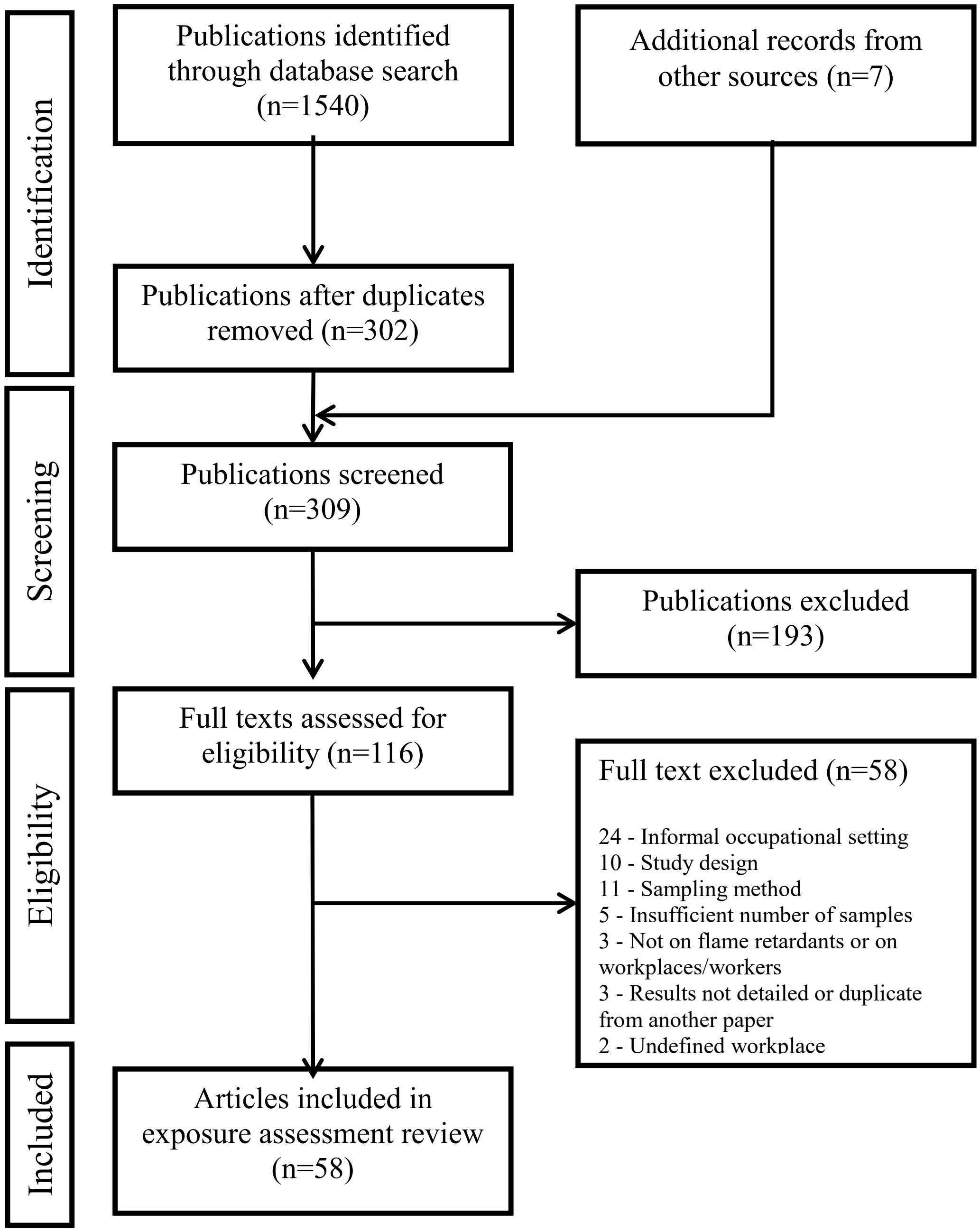
4.3.3. Data collection

After a preliminary assessment of the relevance of each study from the summary by one reviewer (SG), full texts of the selected publications were obtained. Eligibility was assessed independently by two reviewers (SG and FL), and disagreement was resolved by consensus. A data extraction sheet was developed, tested with the first 10 references, then revised to finally include: publication year and country where the study was conducted, aim of the study, methodological characteristics (sample size and study design), media used for exposure assessment (air, dust, serum, urine), FRs assessed, reported exposure data, data analysis preparation (censored data imputation method, reporting of the percentage of values below the limit of detection, etc.) and statistical analyses. Results were extracted for the most commonly cited FRs by one reviewer (SG) and a sample of 10% of articles was checked by a second reviewer (FL). They comprised, for PBDEs: congeners BDE47, BDE183 and BDE209; for NBFRs: hexabromocyclododecane and TBBPA; for chlorinated FRs: syn- and anti-dechlorane Plus; and for OPs: TDCiPP and TPhP (or corresponding major urinary metabolites bis-(2-chloroisopropyl) phosphate and diphenyl phosphate.

4.3.4. Statistical analyses

For FRs with detailed data available in the articles, additional central tendency metrics (geometric mean, arithmetic mean and standard deviation) were calculated when >50% of measures were above the limit of detection (otherwise these metrics were not calculated and the FR was not reported), using either the substitution method for censored data mentioned in the paper, or the value 0 if not specified (Batterman et al. 2010; Schecter et al. 2010; Schindler et al. 2014; Strid et al. 2014; Thomsen et al. 2007; Thuresson et al. 2005). When means were available for BDE47, BDE183 and BDE209 (respectively the main congener in commercial formulations of penta, octa and deca-BDEs), weighted means were compiled for similar workplace groups. PBDE congener profiles were also calculated as percentage of the sum of BDE47, 183 and 209, for blood and dust levels, for which sufficient data were available.

Figure 4.1. Flow diagram of study selection



4.4. Results

4.4.1. Study selection

The flow diagram of study selection is available in Figure 1. Three hundred and nine articles were screened and of those, 116 were obtained and read throughout to assess eligibility. Fifty-eight studies, published between 1999 and July 2018, reported exposure to FRs in workplaces, with a sampling approach that met our inclusion criteria. Thirteen studies took place in China, twelve in the United States, 10 in Sweden, 3 in Taiwan and 3 in the United Kingdom, 2 of each in Finland, Germany, Norway, South Korea and Thailand, and one of each in Belgium, Canada, Denmark, India, Pakistan, and South Africa. One was not attributed to a specific country because it took place in aircrafts, during flights (Allen et al. 2013b). The main reasons for exclusion of studies were that the workplace studied was informal (mostly rudimentary e-waste recycling; n=24), or that the sampling method or the matrix sampled did not meet selection criteria (e.g. passive air sampling, bulk dust sampling in vacuum bags, hair samples, clothing samples; n=14). All excluded studies are listed in Supplementary Table 4.3, with the reason for their exclusion.

4.4.2. Characteristics of selected studies

References of the studies included in this review, as well as the countries, workplaces, sampling media, sample sizes and the chemical class of FRs are listed in Table 4.1. Some occupational settings were more studied than others, such as offices (16 studies) and electronic waste (e-waste) recycling (15 studies). Aircrafts, classrooms and daycare centers were also the focus of several studies, as well as various manufacturing industries. Polybrominated diphenyl ethers were the most commonly measured, followed by novel brominated, organophosphate, and polychlorinated FRs. The two favoured exposure matrices were blood, with results presented from serum or plasma in 20 studies (23 different occupational settings), and dust in 20 studies as well, in which 16 different occupational settings were sampled mainly by dust vacuuming. Stationary air sampling was used in 16 studies and personal air sampling in six, representing altogether 14 occupational settings. Finally, urinary biomarkers were used in four studies, in six different occupational settings. Most studies analyzed the different sampling media by gas chromatography coupled with mass spectrometry (GC-MS), operated in different modes, including electron impact ionization, and selective ion monitoring, except Bello et al. (2018) and Harrad et al. (2010) who used liquid chromatography-electrospray ionization tandem mass spectrometry.

Table 4.1. Workplaces sampled, country of assessment, number of samples per matrix and group of flame retardants sampled for all references included in the review.

		Number of samples per matrix					Flame retardant				
Workplace	**Country**	**Dust**	**Air(P)**	**Air(A)**	**Blood**	**Urine**	**PBDEs**	**NBFRs**	**OPFRs**	**ClFRs**	**Reference**
Aircraft	United States	40					●	●	●	●	Allen et al. (2013a)
	Several			59			●				Allen et al. (2013b)
	United States				30		●				Schecter et al. (2010)
	Germany					332			●		Schindler et al. (2013)
	Sweden			13	41		●				Strid et al. (2014)
Aircraft maintenance	Germany					10			●		Schindler et al. (2014)
	Sweden		6	9	27		●				Strid et al. (2014)
Carpet layers	United States				3		●[a]				Stapleton et al. (2008)
Catering	China				61		●				Wang et al. (2012)
Classrooms, daycare centers, universities	England	36						●			Ali et al. (2011)
	Pakistan				16		●[a]	●			Ali et al. (2014)
	England	28							●		Brommer and Harrad (2015)
	Sweden	10		20					●		Bergh et al. (2011)
	England	43					●	●			Harrad et al. (2010)
	England			17			●				Harrad et al. (2004)
	China	4					●				Kang et al. (2011)
	Denmark	151							●		Langer et al. (2016)
	Sweden				10		●				Strid et al. (2014)
	China	16							●		Wu et al. (2016)
Clothing store, shopping mall	Pakistan				15		●[a]	●			Ali et al. (2014)
	China	5					●				Kang et al. (2011)
Computer classroom	Taiwan			4			●				Chang et al. (2009)
	Finland			3					●		Makinen et al. (2009)
Computer technicians	Sweden				19		●	●			Jakobsson et al. (2002)
Construction	United States		14			24			●		Bello et al. (2018)
Electronic repair shop or store	South Africa	3					●				Abafe and Martincigh (2015)
	Pakistan				30		●[a]	●			Ali et al. (2014)

Workplace	Country	Number of samples per matrix					Flame retardant				Reference
		Dust	Air(P)	Air(A)	Blood	Urine	PBDEs	NBFRs	OPFRs	ClFRs	
E-waste recycling	South Africa	12					●				Abafe and Martincigh (2015)
	China	30					●	●			Deng et al. (2014)
	India				25		●				Eguchi et al. (2012)
	Canada	7						●			Guo et al. (2018a)
	China			15			●				Guo et al. (2015)
	Sweden				54		●[a]				Julander et al. (2005a)
	Sweden			11			●				Julander et al. (2005b)
	Finland		12	6					●		Makinen et al. (2009)
	Thailand	10					●				Muenhor et al. (2017)
	Sweden		12				●				Pettersson-Julander et al. (2004)
	Finland		45				●	●		●	Rosenberg et al. (2011)
	Sweden				19		●				Sjodin et al. (1999)
	Sweden			6			●	●	●		Sjodin et al. (2001)
	Norway				5		●[a]	●			Thomsen et al. (2001)
	Sweden				25		●				Thuresson et al. (2006a)
E-waste storage facilities	Thailand	25					●	●			Muenhor et al. (2010)
Firestation	United States				101		●				Park et al. (2015)
	United States				12		●	●			Shaw et al. (2013)
Foam recycling	United States				12		●[a]				Stapleton et al. (2008)
Furniture workshop	Finland		2	7					●		Makinen et al. (2009)
Gymnastic training facility	United States	12[b]					●	●	●		Ceballos et al. (2018)
Hospitals, medical clinics	Taiwan	9					●				Chou et al. (2017)
	China	16					●				Kang et al. (2011)
	Sweden				20		●				Sjodin et al. (1999)
Hotels	China					26		●			Tao et al. (2018)
Laboratory	Norway				5		●[a]	●			Thomsen et al. (2001)
Leather factory	China				49		●				Wang et al. (2012)
Manufacturing of cables	Sweden				19		●				Thuresson et al. (2005)
Manufacturing of circuit board	Finland		4	6					●		Makinen et al. (2009)
	Sweden			6			●	●	●		Sjodin et al. (2001)
	Norway				5		●[a]	●			Thomsen et al. (2001)
	China	36		36				●			Zhou et al. (2014)
Manufacturing of Dechlorane plus	China				35					●	Zhang et al. (2013)

		Number of samples per matrix					Flame retardant				
Workplace	**Country**	**Dust**	**Air(P)**	**Air(A)**	**Blood**	**Urine**	**PBDEs**	**NBFRs**	**OPFRs**	**ClFRs**	**Reference**
Manufacturing of electric appliances and electronics	Taiwan	14					●	●			Chou et al. (2017)
	China	6					●				Kang et al. (2011)
	China				194		●				Wang et al. (2012)
Manufacturing of expandable polystyrene	Norway		30		20			●			Thomsen et al. (2007)
Manufacturing of furniture, toys and textiles	China	4					●				Kang et al. (2011)
Manufacturing of rubber	Sweden				11		●				Thuresson et al. (2005)
Offices	Belgium	6						●			Ali et al. (2011)
	United States	12		31			●	●			Batterman et al. (2010)
	Sweden	10		20					●		Bergh et al. (2011)
	England	61							●		Brommer and Harrad (2015)
	United States	30				29			●		Carignan et al. (2013)
	China			6			●				Chen et al. (2008)
	China	20					●				Kang et al. (2011)
	China	92					●				Li et al. (2015)
	United States				137		●[a]				Makey et al. (2016a)
	China			18			●	●			Newton et al. (2016)
	Sweden				20		●				Sjodin et al. (1999)
	Sweden			4			●	●	●		Sjodin et al. (2001)
	Sweden				21		●				Strid et al. (2014)
	United States	31			31		●				Watkins et al. (2011)
	United States	31[b, c]	31				●				Watkins et al. (2013)
	China	23							●		Wu et al. (2016)
	China			10							Yang et al. (2014)
Slaughterhouse	Sweden				17		●				Thuresson et al. (2005)
Vehicle dismantling factories	Taiwan			6			●				Gou et al. (2016)
Vehicle parking	China			27			●			●	Li et al. (2016)
Vehicles	England	21							●		Brommer and Harrad (2015)
	United States	20							●		Carignan et al. (2013)
Waste incinerator	South Korea				13		●[a]				Kim et al. (2005)
	South Korea				30		●[a]				Lee et al. (2007)

4.4.3. Sampling approach

Stationary air samples were collected on nine different types of substrates among 22 studies, the most common being a cartridge containing polyurethane foam and a glass fiber filter in 8 of them. XAD-2, a hydrophobic copolymer of styrene-divinylbenzene resin, was used as the absorbent in six of the studies, either using home-made sampling tubes (n=2 studies), or Occupational Health and Safety Administration (OSHA) versatile samplers (OVS) (n=4). Air sampling parameters of the selected studies are listed in Table 4.2.

Environmental sampling methods were very diverse, and this was especially true for settled dust. Dust was almost exclusively collected via vacuum sampling except for two studies that used surface wiping as well (Ceballos et al. 2018; Watkins et al. 2013). Some characteristics of the methods employed for dust vacuuming are listed in Supplementary Table 4.4. Of the 19 studies that sampled settled dust, only five detailed their method, with the type of vacuum cleaner used, the collection apparatus fitted to the vacuum nozzle (or the use of the vacuum bag itself), and a description of the surface and area being sampled (Bergh et al. 2011; Kang et al. 2011; Li et al. 2015; Muenhor et al. 2010; Muenhor et al. 2017).

Biological monitoring of FRs was performed in either blood or urine, depending on the chemicals. Brominated and chlorinated FRs are thought to undergo minimal metabolic transformation and therefore the parent compounds are measured directly in serum or plasma (Genuis et al., 2017; Sales et al., 2017). Most blood concentrations were adjusted on total blood lipids, but Wang et al. (2012) presented results as ng/ml of serum, and Eguchi et al. (2012) in pg/g wet weight of serum. Organophosphate molecules are, on the other hand, rapidly metabolised and their metabolites can be measured in urine within a few hours (Hou et al., 2016). Carignan et al. (2013) and Tao et al. (2018) presented urinary concentrations adjusted on urine's specific gravity, whereas Schindler et al. (2013) reported unadjusted results (but still showed the creatinine content of urine) and Schindler et al. (2014) presented both unadjusted results and results adjusted on creatinine. The majority of selected studies (n=46/58) had an exposure assessment primary endeavour. The others focused mostly on other objectives (e.g. methodological developments or health risk assessment) but still presented exposure data. The lowest and highest detected means, and the highest maxima for each sampling matrix are presented in Table 4.3. The metrics presented and their level of detail varied greatly between studies, which complicated their comparison: some studies presented medians with detailed quartiles, means with or without standard deviation, with or without a range, or geometric means and geometric standard deviations. Moreover, of the 52 studies that reported some values below the detection limit, 39 specified their imputation approach used in statistical analyses of the data, and only 29 presented the percentage of censored data for each FR.

Both highest means and maxima of FRs for BDE209, TPhP and TBBPA were reported in the e-waste recycling industry and in manufacturing of printed circuit boards (Table 4.3). Regarding dust concentrations, the highest mean dust concentrations were found in e-waste recycling facilities for BDE47, BDE183 and BDE209, and in automobiles for TPhP and TDCiPP, whereas the highest values were found in aircrafts for hexabromocyclododecane (HBCDD), and in the dust inside an office computer case for TBBPA. Finally, firefighters, waste incinerators and cable manufacturing workers had the highest means of blood BDE47, BDE183 and BDE209 levels, respectively. Firefighters also had the highest blood TBBPA mean.

Proportions of BDE47, BDE183 and BDE209 over the sum of the three congeners are presented in Figure 2a for blood levels and in Figure 2b for dust levels, by type of workplaces. Overall, BDE47 and BDE183 are found in higher proportions in blood than in dust, in which BDE209 predominates.

Nine studies reported on more than one exposure medium, providing the possibility to compare concentrations measured in different media. Watkins et al. (2013) and Batterman et al. (2010) showed moderately to highly correlated dust and air PBDE concentrations (Spearman correlation; PentaBDE: $r=0.60$, $p=0.0003$; BDE-47, 99, and 100: $r=0.59$ to 0.92), especially for the more volatile PBDEs that have a smaller number of bromine atoms. Positive correlations between dust and air concentrations of OPEs were reported (F-test for goodness of fit statistically significant; linear model R^2: tris(2-chloroethyl) phosphate (TCEP)= 0.5; tris(2-chloroisopropyl)phosphate (TDCiPP)= 0.4; dibutyl phosphate (DBP)= 0.2), whereas

TBBPA was found almost exclusively in dust and not in air (ratio of log[concentration in dust/conc. in PM_{10}] ranging from 0.71 to 3.57) (Bergh et al. 2011; Zhou et al. 2014). Concentrations in biological matrices did not correlate well with those in dust or air samples, aside from a positive trend between urinary bis(1,3-dichloro-2-propyl) phosphate (BDCiPP) and its parent compound TDCiPP in office dust (Spearman $r = 0.45$, $p = 0.02$) (Carignan et al. 2013). Ali et al. (2014) also found significant correlations between lower brominated congeners in dust and plasma (Spearman $r = 0.64$, $p < 0.01$).

Only one study presented results according to particle size. Yang et al. (2014) used an eight-stage cascade impact or to sample 10 OPEs in the air of offices. They showed that TCEP, tri(chloropropyl) phosphate (TCPP), Tri-n-butyl phosphate (TnBP), and TPhP were adsorbed to particles with a mass median aerodynamic diameter greater than 2.5 µm, that tri n-propyl phosphate (TnPP), tributoxyethyl phosphate (TBEP), and 2-ethylhexyl diphenyl phosphate (EHDPP) were in the 1.0−2.5 µm range and that TDCiPP, tricresyl phosphate (TCrP), and tri(2-ethylhexyl) phosphate (TEHP) were mostly distributed in particles of diameters <1 µm. Julander et al. (2005b), used different air samplers to determine the concentrations of PBDEs according to three airborne dust fractions: total (open faced 25-mm cassette), inhalable (particles smaller than 100 µm) and respirable (particles smaller than 10 µm), in an e-waste recycling facility. All measured congeners were found in higher concentrations in the inhalable dust fraction, compared to the respirable fraction, demonstrating the association of PBDEs with the larger airborne particles (Julander et al. 2005b). Two additional studies that reported separately concentrations of the particle and gaseous phases of PBDEs, in offices and in a vehicle parking lot, showed that most congeners were found in the particulate phase, the less brominated congeners having the highest proportion measured in the gaseous phase (Guo et al. 2015; Li et al. 2016). Dechlorane Plus was also found mostly in the particulate phase (Li et al. 2016).

Table 4.2. Air sampling methods used in all references included in the review.

Ref	Substrate	Pump	Flow	Sampling time
Allen et al. (2013b)	Sorbent tube (SKC No. 226-143) and in-house-prepared glass cartridges; XAD-2 and polyurethane foam	Not mentioned	1.5 to 8.6 l/min	Not mentioned
Batterman et al. (2010)	Polytetrafluoroethylene filters (47 mm dia, 1 μm pore size) (SKC Inc.), followed by pre-cleaned polyurethane foam (22×76 mm, SKC, Inc.), in custom glass cartridges.	Not mentioned ("Medium-flow sampling systems")	15 l/min	One week
Bello et al. (2018)	• Aerosol dust : IOM inhalable sampler (25-mm quartz filter) • CIP 10-M rotating cup bioaerosol sampler with solution of butyl benzoate containing 5mM 1-(9-anthracenylmethyl) piperazine	• GilAir 3 (Sensidyne) • CIP-10MI sampler (Arelco, Fontenay-Sous-Bios Cedex, France)	2 L/min 10 L/min	15 to 176 min
Bergh et al. (2011)	Solid-phase extraction cartridges (IST, Hengoed, UK); aminopropyl silica	AC-powered pump (N026.1.2AN.18; KNF Neuberger, Germany)	Not mentioned (max. of ~2m³/h according to manufacturer)	8h
Chang et al. (2009)	Modified total suspended particulate inlet; polyurethane foam and glass fiber filter	PS-1 high volume air sampler (General Metal Works, USA)	250 L/min	24h
Chen et al. (2008)	Polyurethane foam and glass fiber filter	High-volume sampler	400-700 L/min	8-10h
Gou et al. (2016)	Glass cartridge; polyurethane foam and quartz fiber filter	PS-1 sampler (Graseby Andersen, GA, USA)	225 L/min	40h
Guo et al. (2015)	Polyurethane foam plugs (60cm diar×51mm length, SKC Inc.) and glass fiber filter (90mm dia, pore size 0.1μm, SKC Inc.)	High-volume sampler model (TE-100, Tisch, USA) 3 middle volume samplers (Lao Ying 2030, Qingdao Laoshan electronic instrument factory Co. Ltd., China)	220–280 L/min 100 L/min	8h

Ref	Substrate	Pump	Flow	Sampling time
Guo et al. (2018a)	ORBO sampler: glass fiber filter (pore size 0.7 µm) with polyurethane foam (PUF/XAD/PUF, Sigma-Aldrich)	Low-volume air samplers	5.5-10 L/min	8-30h
Harrad et al. (2004)	Total suspended particulate inlet modified to hold a teflon-coated glass fiber filter (pore size 0.6 µm) and precleaned polyurethane foam plugs (0.016 g cm-3, 827 cm^3)	High-volume sampler (Graseby Andersen, GA, USA)	600-800 L/min	Depending on room volume (max. 24 h)
Julander et al. (2005b)	Open-face 25 mm cassette; SKC 2 aluminium cyclone, 25-mm cassette; IOM inhalable dust sampler, 25-mm cassette All used with cellulose acetate filters	Not mentioned	2 L/min	16h
Li et al. (2016)	Glass fiber filter (20.3× 25.4 cm, Whatman) and polyurethane foam (90× 65 mm id.) plug	High-volume sampler	Not mentioned	4,5-24h
Makinen et al. (2009)	OSHA Versatile Samplers (filter + XAD resin and polyurethane foam) IOM sampler (Glass fiber filters)	Personal pumps (SKC 224, SKC Ltd.)	0,98-1,05 L/min (OVS) 1,95-2,08 L/min (IOM)	119-663 min
Newton et al. (2016)	Glass fiber filters from Pall Corp., MI, USA (binder-free A/E borosilicate, 25 mm diameter) and Polyurethane foam plugs from Specialplast AB, Gillinge, Sweden (diameter 15 mm, thickness 15 mm)	Low volume pump	5 L/min	• 2.5 h/day for 28 days • 2.5 days cont.
Pettersson-Julander et al. (2004)	Modified version of NIOSH method 0500 ‘‘Particulates, not otherwise regulated’’, sampler with pre-washed XAD-2 adsorbent, and a cellulose pad onto which a glass fibre filter was placed	Personal sampling pumps	2 L/min	8h
Rosenberg et al. (2011)	OSHA Versatile Samplers (no. 226-30-16, SKC Ltd): glass fibre filter + 2 XAD-2 resin layers (270 and 140 mg), separated by PUF plugs	Not mentioned	2,5 L/min	191-408 min

Ref	Substrate	Pump	Flow	Sampling time
Sjodin et al. (2001)	Anodized aluminum sampler, 25-mm, binder-free A/E borosilicate glass fiber filter (Gelman Sciences Inc.), 2 polyurethane foam plugs (15mm diam. and thickness (Special last AB)	Personal pump (224-PCXR7, SKC Inc., Eighty Four, PA)	3 L/min	500 min
Strid et al. (2014)	OSHA Versatile Samplers: glass fiber filter, two XAD-2 adsorbent layers (separated by polyurethane foam)	Not mentioned	3 L/min	8h
Thomsen et al. (2007)	Total dust: 25 mm black Gelman cassettes (no. 4376, Pall) and 25 mm glass fiber microfiber filters (1.6 µm pore size, no. 1820 025, Whatman), Millipore absorbent pads (no. AP1002500, Billerica).	In-house-made pumps	2 L/min	8h
Watkins et al. (2013)	Glass tube casing; glass fiber filter (pore size 1 µm) with polyurethane foam plug (76 mm).	Sampling pump	4 L/min	48h
Yang et al. (2014)	Cascade impactor; Glass fiber filters	Anderson eight-stage nonviable cascade impactor with a back-up filter (Tisch Environmental, Cleves, USA)	28,3 L/min	48h
Zhou et al. (2014)	Pre-baked glass fibre filters (11 cm dia).	Median-volume samplers	100 L/min	8h

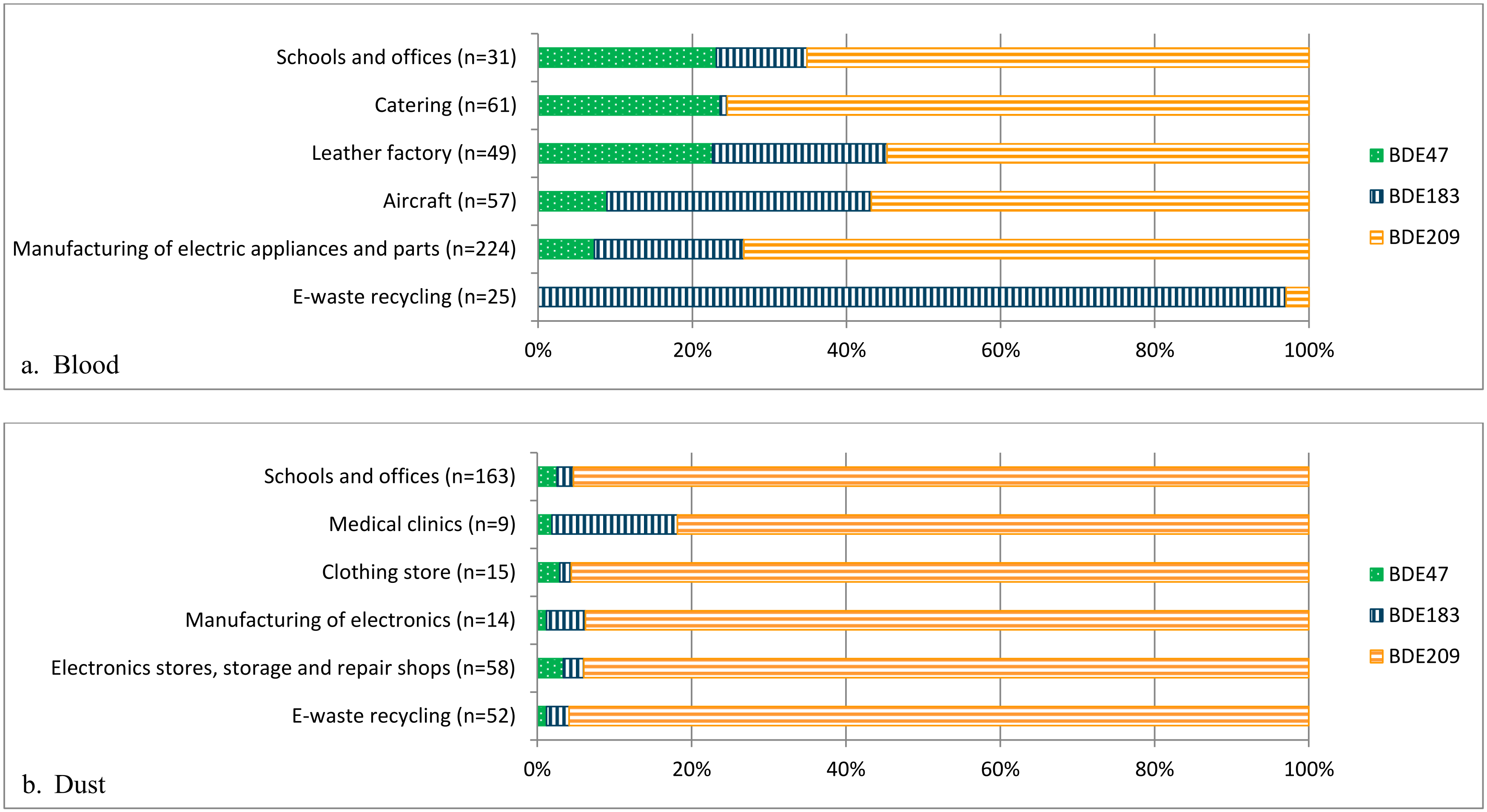
Table 4.3. Summary of the reported highest means and maxima for brominated and organophosphate esters flame retardants, in dust, air and blood

Substance	Reported concentration[a] Lowest detected mean	Highest mean	Highest max	Workplace (process or task)	Country	Reference
Air (ng/m^3)						
BDE47	0.014			Vehicle dismantling factories (Daytime)	Taiwan	Gou et al. (2016)
		343		E-waste recycling (Printed wiring board heating)	China	Guo et al. (2015)
			42.8	Aircraft maintenance	Sweden	Strid et al. (2014)
BDE183	0.001			Computer classroom	Taiwan	Chang et al. (2009)
		19.5		E-waste recycling	Finland	Rosenberg et al. (2011)
			98.0	Aircraft	International	Allen et al. (2013b)
BDE209	0.0023			Computer classroom	Taiwan	Chang et al. (2009)
		2 170		E-waste recycling (Crushing)	China	Guo et al. (2015)
			2 100	Aircraft	United States	Allen et al. (2013b)
TPhP	0.1			Daycare	Sweden	Bergh et al. (2011)
		850[b]	10 300	E-waste recycling	Finland	Makinen et al. (2009)
TDCiPP	2.25			Offices	China	Yang et al. (2014)
		90[b]	450	E-waste recycling	Finland	Makinen et al. (2009)
TBBPA	0.0121			Offices (Vapour phase)	United States	Batterman et al. (2010)
		1 150		Manufacturing of circuit boards (Lamination)	China	Zhou, 2014
			14 600	E-waste recycling	Finland	Makinen et al. (2009)
ΣHBCDD	0.087			Office (Low use)	China	Newton et al. (2016)
		48		Aircraft	Sweden	Strid et al. (2014)
			963	Aircraft maintenance	Sweden	Strid et al. (2014)
Dust (ng/g)						
BDE47	1.79			Office floor dust	China	Li et al. (2015)
		6 240		E-waste recycling (Coarse crushing room)	China	Deng et al. (2014)
			23 000	E-waste recycling (Dismantling)	Thailand	Muenhor et al. (2017)
BDE183	1.00			Clothing store	Pakistan	Ali et al. (2014)
		22 100[a]		E-waste recycling (Shredding wires)	China	Deng et al. (2014)
			12 970[a]	Office floor dust	United States	Watkins et al. (2011)
BDE209	65.0			Clothing store	Pakistan	Ali et al. (2014)

Substance	Reported concentration[a] Lowest detected mean	Highest mean	Highest max	Workplace (process or task)	Country	Reference
		665 000		E-waste recycling (Shredding wires)	China	Deng et al. (2014)
			2 600 000	Aircraft (Vent dust)	United States	Allen et al. (2013a)
TPhP	88			Clothing store	Pakistan	Ali et al. (2014)
		15 000	170 000	Vehicle	UK	Brommer and Harrad (2015)
TDCiPP	11			Clothing store	Pakistan	Ali et al. (2014)
		110 000	740 000	Vehicle	UK	Brommer and Harrad (2015)
TBBPA	223			Office floor dust	United States	Batterman et al. (2010)
		6 940	9 010	Office (Dust in computer case)	China	Li et al. (2015)
ΣHBCDD	8 900	8 900		Classrooms	UK	Harrad et al. (2010)
			1 100 000	Aircraft (Carpet)	United States	Allen et al. (2013a)
Blood (ng/g lipids)						
BDE47	0.26			Catering	China	Wang et al. (2012)
		52		Firestation	United States	Shaw et al. (2013)
			540	Foam recyclers	United States	Stapleton et al. (2008)
BDE183	0.148			Manufacturing of cable (Measurements)	Sweden	Thuresson et al. (2005)
		4.12		Waste incinerator	South Korea	Kim et al. (2005)
			18.7	E-waste recycling	Sweden	Sjödin et al. (1999)
BDE209	0.75			Leather factory	China	Wang et al. (2012)
		52.4	268	Manufacturing of cables (Miscellaneous)	Sweden	Thuresson et al. (2005)
TBBPA	0.34			Laboratory	Norway	Thomsen et al. (2001)
		27	88	Firestation	United States	Shaw et al. (2013)
ΣHBCDD	162	218		Manufacturing of expandable polystyrene	Norway	Thomsen et al. (2007)
Urine (µg/l, adjusted on specific gravity)						
DPhP	0.21[b]			Hotel	China	Tao et al. (2018)
		3.31[c]		Aircraft maintenance	Germany	Schindler et al. (2014)
			302[c]	Airline workers	Germany	Schindler et al. (2013)
BDCPP	0.24[b]			Hotel	China	Tao et al. (2018)
		408	1760	Office	United States	Carignan et al. (2013)

[a] Deng et al. (2014) did not report the range of values, but they probably found a higher maximum value than Watkins et al. (2011).
[b] Geometric mean
[c] Unadjusted

Figure 4.2. Congener profiles in blood (a) and dust (b), presented as the percentage of the sum of congeners BDE47, BDE183 and BDE209 based on weighted means, by type of workplaces



4.5. Discussion

This review is, to our knowledge, the most extensive appraisal of occupational exposure to FRs. The 58 collected peer-reviewed studies attest a growing interest in exposure assessment of these substances in occupational settings, throughout the last two decades. Studies focused more on older FRs (PBDEs and OPEs), and much less on NBFRs and ClFRs, possibly reflecting less concern on the potential health effects of the latter, as well as developing analytical methods for these compounds. PBDEs are also the most commonly found FRs in home dust, even decades after a phase-out in response to health concerns that raised the interest of researchers to identify sub-populations that remain highly exposed (Coelho et al. 2014). As pertinent analytical aspects of PBDEs and NBFRs have been previously reviewed (Covaci et al. 2011; Fulara and Czaplicka 2012), they are not discussed further here.

Workplaces in a few industrial sectors had high values for several FRs. E-waste recycling, air transportation and manufacturing facilities are among workplaces with the highest levels of FRs. E-waste recycling exposes its workers especially during dismantling operations of old electric and electronic equipment, in which several kinds of FRs are found (Ceballos et al. 2015; Schluep et al. 2009). For example, the dust inside a TV cabinet has been found to contain up to 2-3 orders of magnitude more PBDEs than household dust (Takigami et al. 2008), partly explaining such high exposures in e-waste workers. As for the air transportation sector, aircraft constructors have to abide by some of the strictest fire safety standards, increasing the use of FRs (Federal Aviation Administration 2009). Finally, firefighters' protective equipment and vehicles are treated with FRs, adding to their background exposure (Alexander and Baxter 2016).

Many different workplaces were investigated, but the tasks/activities or specific workplace areas were not always described comprehensively, which hinders the identification of determinants of exposure. On the other hand, studies that presented a detailed description of tasks or sampled areas had a small sample size, which reduced their power to bring out specific determinants (e.g. in Deng et al. (2014) or Zhou et al. (2014)).

4.5.1. Sampling approach

FRs are semi-volatile organic chemicals (SVOCs), defined by their vapour pressure typically between 10 and 10^{-6} pascals (Pa), allowing them to be airborne in both vapour and particle phases (Bidleman 1988), which explains the selection of sampling methodologies that allowed collection of both phases.

Numerous sampling methodologies exist for SVOCs and generally rely on filtration (e.g. Teflon and glass or quartz fibers) and sorption (e.g. XAD-2, polyurethane foam and combination of the two) for particle and gaseous phase compounds respectively (Krol et al. 2011). This combined sampling approach is considered a standard method for several SVOCs such as pesticides and polycyclic aromatic hydrocarbons (Kim and Soderholm 2013). A European standard now establishes the requirements for SVOC method validations and an ISO standard is currently in development (European Committee for Standardization 2014). Methods used to evaluate exposure to FRs in occupational settings should hence be developed in accordance to the published or coming international standards.

Caution is advised when comparing results between studies in which methodologies were not optimized for SVOC sampling such as those using filtration only (Julander et al. 2005b; Yang et al. 2014; Zhou et al. 2014). Filtration-only methods may be associated with important underestimation due to particle-phase evaporation under certain circumstances (Kim 2010; Melymuk et al. 2014), a phenomenon that may be exacerbated by the use of higher flow rates, such as the ones used in ambient air sampling by Harrad et al. (2004) (600-800L/min), and by long sampling durations. Due to these limitations, the gas-particle partition of an airborne contaminant cannot be calculated with exactitude by a sampling assembly consisting of a filter and sorbent. Nonetheless, the methods used by Guo et al. (2015) and Li et al. (2016) can still provide a reasonable estimate of the gas-particle partition of the FRs sampled.

The concentration of FRs in settled dust is often considered to be a proxy for their internal dose, thereby assuming significant skin permeation, hand-to-mouth behaviour or unintentional dust ingestion in workers (American Industrial Hygiene Association 2015; Frederiksen et al. 2009; Gorman Ng et al. 2016). None of the settled dust exposure assessment methods followed a standard procedure across the studies; this was also mentioned in a systematic review on the associations between internal dose of PBDEs and indoor dust (Bramwell et al. 2016). Among major parameters to be taken into account when collecting dust, the sampling method itself, the sample storage and its preparation (sieving) are critical for sample stability (Allen et al. 2008; Mercier et al. 2011). Vacuuming can be an efficient way to capture semi-volatile compounds associated with dust particles, and can allow for gravimetric analyses, as mentioned in the Standard practice for collection of floor dust for chemical analysis (ASTM international 2014). This dust collection method, developed by the US-EPA, was widely used in home dust exposure assessments (Mercier et al. 2011), but none of the studies included in the present review referred to it. This is unfortunate, as many factors can affect the efficiency of particles collection, such as the distance between the nozzle and the vacuumed surface, the flow rate, the characteristics of the sampled surface, and the collection apparatus itself (filter, nylon sock, cyclone, etc.) (ASTM international 2016; Roberts et al. 1996). Many studies that were excluded for methodological reasons collected bulk dust by sweeping surfaces with a brush or sampling directly from vacuum bags, approaches that are hardly reproducible and reliable. As with air sampling methods, the use of a filter only to collect dusts may result in an underestimation of measurements. Surface wiping has been shown to be a reliable way to quantify the presence of a semi-volatile on a given surface, when carried following a strict protocol (Jung 2014). However, method validations have yet to demonstrate the quantitative transfer of FRs from the sampled surface to the final extract in the laboratory to obtain a reproducible yield without bias (due, for instance, to strong chemical bond between contaminants and sampled surface or intermediate containers during storage). Moreover, the sampling location also has an impact on the potential transfer to humans, be it floor dust or the inside of a computer case (Allen et al. 2008). Dust may remain a useful non-invasive matrix for exposure assessment in workplaces, but standardized and reproducible methods should be used, such as utilizing a standard template for wipe sampling, or following a standard protocol for vacuuming and thoroughly detailing sampled surfaces and locations.

4.5.2. Study results

The association between air and dust content of FRs in various settings has not been consistently established in the reviewed studies. Atmospheric conditions, the sampling flow rate and duration, as well as the molecule's intrinsic properties, can influence the particle:gas partition and can partly explain the variability in the associations between the sampling matrices (Liagkouridis et al. 2014; Ward and Smith 2004). For instance, some industrial sectors use heating processes or hot temperatures, such as smelters and ovens, where the particle:gas partition would differ greatly from the partition in industries with more temperate workplaces (Guo et al. 2015). Occupational exposure assessments have to be performed with a device that collects both the particle and vapour phases, rather than only using settled dust, to adequately assess the potential inhalation exposure to such semi-volatile FRs. More studies are needed to describe the particle-size distributions of FR particles, as it may assist in understanding exposure and guide prevention efforts.

Biological monitoring of FRs in workers, although used frequently in the reviewed research studies, would generally not be recommended for occupational exposure surveillance, particularly because the biological half-life of most FRs is not well documented, limiting inferences from measured concentrations in blood or urine (Szabo et al. 2010; Tao et al. 2018; Thuresson et al. 2006b). However, it can provide valuable insight when compared to levels in the general population, especially as most FRs are not regulated. Biological monitoring also takes into account all routes of exposure, allowing validation of the hypothesis that ingestion is a non negligible exposure pathway, when coupled with other exposure assessment matrices (Covaci et al. 2011; Watkins et al. 2011). As for previously mentioned exposure assessment methods, biomarker measurements were also not presented in a standardised way. Most results of blood concentrations were presented on a total blood lipid content basis, which is considered to reflect the body burden of lipophilic substances, and enables comparisons between populations (Rylander et al. 2006). One epidemiology study (Eguchi et al. 2012) appropriately presented results on a serum wet weight basis, which may be less prone to bias than lipid adjustment for use in an epidemiology study (Schisterman et al. 2005). One study did not present results adjusted on lipids or wet weight, which impedes comparison of concentrations in these workers with others' (Wang et al. 2012). The same applies for urinary metabolites of OPEs, generally adjusted on urinary specific gravity, which is minimally impacted by age, body composition, urine flow, physical activity and other factors, as opposed to creatinine (Boeniger et al. 1993). This is especially true if the sampled population works in a warm environment and with limited access to restroom breaks, leading to more concentrated urine and hence, overestimated levels. All of the studies included in this review specified the time of the day at which urine samples were taken (after work), which is important for rapidly metabolized molecules such as OPEs (Hou et al. 2016).

Only about a third of the studies had sample sizes above 30, which explains that their statistical analyses are essentially descriptive. Nevertheless, it is fundamental to report the limits of detection and quantification, the proportion of data that falls below those limits, and the approach used to handle the non-detected data in analyses (imputation/substitution rules or exclusion) for the reader to grasp the overall distribution of the exposure (IT Environmental Programs Inc. and ICF Kaiser Incorporated 1994). Several statistical approaches were proposed in recent years to adequately analyse censored data and they all recommend avoiding simple substitution methods to reduce bias (Dinse et al. 2014; Helsel 2010; Lavoue et al. 2019; Lubin et al. 2004). Statistical comparisons of concentrations between studies were quite challenging, as some articles did not present standard deviations or sometimes no means at all (arithmetic or geometric). Few articles presented geometric means, while occupational exposure data is generally recognized to be log-normally distributed (Waters et al. 2015). Finally, some articles even lacked a "Statistics" or a "data analysis" section in their methodology.

Among the FRs reported in our study, only triphenyl phosphate (TPhP) has an occupational threshold limit value (TLV) that would allow identification of workplaces needing urgent intervention. The TLV for TPhP of 3 mg/m^3, established to prevent skin irritation and neurotoxic effects (American Conference of Governmental Industrial Hygienists 2019), is quite high and none of the workplaces surveyed presented such values. The highest maximum for TPhP was recorded in e-waste recycling, at 0.5% of the TLV (Makinen et al. 2009). In the absence of an exposure standard, Haines et al. (2017) derived a biomonitoring reference value for BDE47 of 67 ng/g lipids based on the 95th percentile of Canadian population serum values of PBDEs; several occupational groups show maximal values exceeding this level, such as office workers, airline workers, firefighters, carpet layers and foam recyclers (Makey et al. 2016a; Schecter et al. 2010; Shaw et al. 2013; Stapleton et al. 2008). Regarding median values, firefighters in the United States had median concentrations of BDE47 exceeding those of the general population workers from both the United States (19.4 ng/g lipids) and Canada (9.1 ng/g lipids) (Gravel et al. 2018).

The distribution profiles of the three main PBDEs according to sampling media can provide insight on avenues for exposure prevention. Some workplaces show a greater exposure to less brominated FRs, attesting to the presence of the commercial formulation PentaBDE, which has been found to be bioaccumulative and toxic (Dishaw et al. 2014). Schools and offices showed high levels of lower brominated PBDEs and would benefit from adequate ventilation to decrease the exposure of workers to these more volatile substances. On the other hand, workplaces where BDE209 is more prevalent in dust would benefit from a thorough cleaning and dusting, as this congener is less volatile and adsorbed mainly to dust. The proportions of the same congeners in blood show that although BDE209 is thought to be less bioaccumulative (Frederiksen et al. 2009), it is still highly prevalent in workers of all studied occupations, meaning that exposure to the commercial formulation DecaBDE is widespread.

Finally, table 4.4 lists several gaps that were identified in the body of literature and offers some recommendations to overcome them in the conduct of comprehensive occupational exposure assessments.

4.5.3. Strengths and limitations of the systematic review

This is the first systematic review on occupational exposure to FRs. The PRISMA protocol was followed to ensure the exhaustiveness and the reproducibility of our work. Moreover, the bibliographic databases searched for article selection are considered to be optimal for an adequate and efficient coverage of the literature (Bramer et al. 2017). This review succeeded in identifying industrial sectors that would benefit from further investigation of exposure to

FRs and reduction measures. Gaps in the body of literature were also identified and recommendations were made to improve the strength of future studies on the matter.

Some limitations of this review need to be mentioned. It is difficult to assess the representativeness of the occupational exposure data presented here, as companies that welcome a research team into their facilities are probably more likely to be proactive in exposure prevention, and hence exposure levels in their premises are possibly not the most problematic. In the reviewed body of literature, the variety of experimental approaches limits the inference to their respective industrial sectors. Additionally, a whole body of literature on informal occupational settings was excluded from this review; FR concentrations in such uncontrolled conditions are not comparable to those in formal settings and probably need more attention from a general public health perspective than an occupational health point of view. Non peer-reviewed papers and grey literature were excluded, which may have reduced the available data, although it ensured a minimal degree of confidence in the results. Finally, most of the extraction of data was done by one reviewer, although a second reviewer checked a small proportion of the extracted data, which may have introduced difficult to quantify errors.

Table 4.4. Research gaps and recommendations on occupational assessment of exposure to flame retardants

Research gaps	Recommendations
There are less studies on more recently introduced flame retardants (novel brominated, organophosphorus and chlorinated) than on polybrominated diphenyl ethers.	Conduct more occupational exposure assessments on novel brominated, organophosphorus and chlorinated flame retardants. Workplaces and tasks should be well defined to help identifying determinants of exposure and ensure comparability between studies.
Settled dust and air sampling methods are not standardised and not sufficiently described to be reproducible. Limitations of dust vacuum sampling methods are not well documented.	A reproducible and standardized vacuuming or wiping dust collection method should be employed. Air sampling methods should be better described and should refer to reference methods developed according to standards such as EN 13936.
Adjustment of concentrations in biological matrices is not systematic (e.g. by lipid or wet weight in blood, specific gravity or creatinine levels in urine).	Standardisation of analysis and reporting of biological monitoring methods is necessary to facilitate interpretation of results across studies.
The associations between flame retardant concentrations in the different matrices are understudied and poorly understood.	More biomonitoring research is needed, coupled with environmental sampling, to understand associations between matrices.
The particle:gas partition of flame retardants is insufficiently documented.	Particle:gas partition is subject to be inaccurate with commonly used sampling methods. A standard method capable to yield an exact partition should be developed. .
The role of the nature of the particle on which flame retardant is adsorbed is not known.	Understand to which extent the nature of the particle has a role in exposure.
Information on the particle-size distribution of the particle-phase FR is scarce.	More research is needed to understand exposure pathways in workers.
Statistical analyses and reporting of results is disparate among the different studies.	Statistical analyses should consider the distribution of the data, and the limits of detection should be taken into account when reporting and analysing the data.
	More research should be undertaken in firefighter and e-waste recycling workers to assess potential adverse health effects associated with higher exposures.

4.6. Conclusion

Some workplaces clearly expose their workers to flame retardants. While methodological inconsistencies among the different reviewed studies rendered exposure assessment difficult, the highest concentrations found in e-waste recycling, air transportation and firefighting warrant more investigation into these workplaces using standard protocols and validated methods. Thorough and reproducible occupational exposure assessments will complement the body of knowledge and support occupational health decision making for protective and preventive interventions.

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4.8. Appendix

Table S4.1. PRISMA 2009 checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Title page
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Introduction par. 1-3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction par. 3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No review protocol exists
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Methods, par. 3-4: Inclusion and exclusion criteria
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Methods, par. 2: Search strategy description
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Table 2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Methods, par. 2: Search strategy description
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Methods, par. 5: Data collection
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Methods, par. 5: Data collection
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A (exposure assessment)
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Methods, par. 5: Data collection
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Methods, par. 6: Statistical analyses

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Discussion, last two par.: Strengths and limitations of the systematic review
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Methods, par. 6: Statistical analyses
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1, Supplementary Table 3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1, Table 2, Table 3, Supplementary Table 4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Discussion, last two par.: Strengths and limitations of the systematic review
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figure 2
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Discussion, par. 1-12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Discussion, last two par.: Strengths and limitations of the systematic review
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Conclusion, Table 4.
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	No external funding than salary from IRSST

IRSST, Institut de recherche Robert-Sauvé en santé et en sécurité du travail; N/A, not applicable; par., paragraph

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Table S4.2. Detailed electronic research strategy and results as of July 2018

Database	Detailed query	Number of hits
Pubmed	(("manpower"[Subheading] OR "manpower"[All Fields] OR "workers"[All Fields]) OR ("occupational exposure"[MeSH Terms] OR ("occupational"[All Fields] AND "exposure"[All Fields]) OR "occupational exposure"[All Fields]) OR ("workplace"[MeSH Terms] OR "workplace"[All Fields])) AND (("flame retardants"[Pharmacological Action] OR "flame retardants"[MeSH Terms] OR ("flame"[All Fields] AND "retardants"[All Fields]) OR "flame retardants"[All Fields]) OR ("pentabromodiphenyl ether"[Supplementary Concept] OR "pentabromodiphenyl ether"[All Fields] OR "pbde"[All Fields] OR "halogenated diphenyl ethers"[MeSH Terms] OR ("halogenated"[All Fields] AND "diphenyl"[All Fields] AND "ethers"[All Fields]) OR "halogenated diphenyl ethers"[All Fields])) NOT ("review"[Publication Type] OR "review literature as topic"[MeSH Terms] OR "review"[All Fields]) AND ("humans"[MeSH Terms] OR "humans"[All Fields]) AND "humans"[MeSH Terms]	**184**
Embase	((((workers or occupational exposure or Workplace) and (flame retardants or pbde)) not review) and humans).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]	**16**
Medline	((((workers or occupational exposure or Workplace) and (flame retardants or pbde)) not review) and humans).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	**128**
Global Health	((((workers or occupational exposure or Workplace) and (flame retardants or pbde)) not review) and humans).mp. [mp=abstract, title, original title, broad terms, heading words, identifiers, cabicodes]	**10**
Web Of Science	TOPIC: ((workers OR occupational exposure OR Workplace) AND (flame retardants OR pbde)) Refined by: DOCUMENT TYPES: (ARTICLE) Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI.	**202**
Google scholar	("flame retardants") (worker | workers | workplace | occupational) (exposure)	**15200***

* Only the first 1000 results could be consulted in Google scholar

Table S4.3. References not retained and reasons for exclusion

Reference	Reason for exclusion	Comment
Alexander and Baxter (2016)	Sampling matrix	Sampling on clothing
Allgood et al. (2017)	n<6	No more than two samples in 7 different occupational settings
Anderson et al. (1978)	Design	No quantitative occupational exposure
Aylward and Hays (2011)	Design	Clinical study of two groups following an industrial accident with PBB
Besis et al. (2014)	n<6	No more than 5 samples in 8 occupational settings
Besis et al. (2016)	Not on workplaces/workers	Outdoor environmental samplings
Bi et al. (2007)	Informal	Inhabitants of an informal e-waste recycling region
Brown et al. (2014)	Sampling method	Dust samples collected from vacuum cleaners
Chen et al. (2009)	Informal	Air in an informal e-waste recycling region
Chen et al. (2015)	Informal	E-waste recycling workers from Longtang, Qingyuan city in Guangdong province
Cheng et al. (2009)	Results not detailed	Results (metrics) not provided per congener
Christiansson et al. (2008)	Sampling method	Dust samples collected by hand
Eguchi et al. (2015)	Informal	Workers at an e-waste recycling site of Bui Dau
Espino and Leon (2014)	Sampling method	Dust particles were scraped from air-conditioner filters into a white paper
Fulong and Espino (2013)	Sampling method	A disposable steel brush was used to collect dust samples
Guo et al. (2015)	Sampling method	Dust collected by brushes, two of the four samples taken inside machinery
Han et al. (2016)	Design	Article on dust deposition
Hassan and Shoeib (2015)	Sampling method/Undefined workplace	Dust samples collected from vacuum cleaners, and workplace undefined
Hazrati and Harrad (2006)	Sampling method	Passive air sampling
He et al. (2016)	Sampling method	Dust collection method on A/C filters not specified
Hearn et al. (2013)	Undefined workplace	Workplaces of participants not reported
Hong et al. (2013)	n<6	Less than 6 offices and 10 other workplaces undefined
Julander et al. (2014)	Not organic flame retardants	Exposure to 20 toxic metals
Kademoglou et al. (2017)	Sampling method	Dust sampled collected from vacuum cleaner bags
La Guardia and Hale (2015)	n<6	One dust and air sample per location, in 4 locations
Leung et al. (2010)	Informal/Design	Milk, placenta and hair samples, and participants are residents of an informal e-waste recycling site
Leung et al. (2011)	Informal/Sampling method	Samples were collected using plastic brushes, and in informal e-waste recycling workshops
Liang et al. (2016)	Informal	Inhabitants of an informal e-waste recycling region
Ma et al. (2011)	Sampling matrix	Hair samples
Makey et al. (2014)	Duplicate results	On temporal variability, results more detailed in Makey, 2016

Reference	Reason for exclusion	Comment
Mandalakis et al. (2008)	Sampling method	Passive air sampling
Marklund et al. (2005)	n<6	No more than 4 samples in a given occupational setting
Qu et al. (2007)	Informal	Residents from e-waste dismantling region
Ren et al. (2009)	Informal	Residents from e-waste dismantling region
Ren et al. (2011)	Informal	Residents from e-waste dismantling region
Ren et al. (2013)	Informal	Uncertain if formal or not, email sent to corresponding author
Schecter et al. (2009)	Design	Analyses from previously published data
She et al. (2010)	Design	Analyses from previously published data
Shen et al. (2015)	Sampling method	Dust sampled collected from vacuum cleaner bags
Thuresson et al. (2006)	Design	Analyses from previously published data
Tue et al. (2013)	Informal	Air in an informal e-waste recycling sites in Hai Phong city
van den Berg et al. (2017)	Not on workplaces/workers	Participants with no known occupational exposure
Wang et al. (2013)	Sampling matrix	Concentrations in different food items
Wang et al. (2010)	Informal	Samples in villages involved in e-waste dismantling
Wolff and Aubrey (1978)	Results not detailed	Results presented are peak area ratios
Xu et al. (2015)	Informal	Samples from family-run workshops
Xu et al. (2016a)	Undefined workplace	Workplaces of participants not reported
Xu et al. (2016b)	Informal	Participants in a rural e-waste area
Yan et al. (2012)	Informal	Participants from e-waste recycling workshops in Longtang Town, Qingyuan County
Yan et al. (2018)	Informal	Participants from e-waste recycling workshops in Qingyuan, mainly from family workshops
Yang et al. (2013)	Informal/Not organic flame retardants	Blood lead levels, in an e-waste dismantling region
Yi et al. (2016)	Design	Air sampling from areas surrounding factories
Yu et al. (2010)	Informal	E-waste recycling sites in Guiyu
Yuan et al. (2008)	Informal	Workers from a village close to an e-waste recycling site
Zheng et al. (2010)	Informal	Participants from e-waste recycling workshops in Longtang Town, Qingyuan County
Zheng et al. (2011)	Informal	Participants from e-waste recycling workshops in Longtang Town, Qingyuan County
Zheng et al. (2014)	Informal	Participants from e-waste recycling workshops in Longtang Town, Qingyuan County
Zheng et al. (2017)	Informal	Workers recruited from an e-waste site in South China

Table S4.4. Dust vacuuming methods used in retained articles

Vacuum cleaner	Collection apparatus/substrate	Vacuumed surface	Reference
LG 1600-W vacuum cleaner	Dust unit	Not specified	Abafe and Martincigh (2015)
Not specified	25µm mesh size nylon sock	1 m² of carpet for 2 minutes 4 m² of hard floor for 4 minutes	Ali et al. (2011)
Not specified	Cellulose extraction thimble	Whole plane carpet Air return grilles	Allen et al. (2013)
Oreck® XL compact canister vacuum	Undefined filter	1 m² area in repeated strokes	Batterman et al. (2010)
Alto AERO 840 industrial strength vacuum cleaner	Cellulose filters	Tops of bookshelves, cupboards, desks, and/or casings of windows and doors at least 0.8 m above the floor	Bergh et al. (2011)
Not specified	25µm mesh size nylon sock	1 m² of carpet for 2 minutes 4 m² of hard floor for 4 minutes	Brommer and Harrad (2015)
Not specified	Cellulose extraction thimble	Entire floor for 10 min	Carignan et al. (2013)
Nilfisk Advance Euroclean UZ934 HEPA canister vacuum cleaner	Not specified	Air-conditioner filters	Chou et al. (2017)
Philips FC6130, 900 W	Not specified	Until sufficient mass (5–10 g) was collected	Deng et al. (2014)
Not specified	Polyester socks	Unspecified surface of floor Top of work benches	Guo et al. (2018)
Not specified	25µm mesh size sock	Entire floor surface of each classroom for 4 minutes	Harrad et al. (2010)
Black & Decker Dustbuster	Vacuum bags	Air-conditioner filters	Kang et al. (2011)
Not specified	ALK dust filters	Non-floor surfaces	Langer et al. (2016)
RO1274, Rowanta, Germany	Vacuum bags	Floors, 0.5 m²/min once a day for 10 days Desk surface, desktop phones, and back cabinets of desktop computers totaling about 7.5 m² Bottom of the interior of 18 computer cases	Li et al. (2015)
Hitachi CV-BL16 1600 W	25µm mesh size nylon sock	4 m² of bare cement floor for 4 minutes	Muenhor et al. (2010)
Hitachi CV-BM16 RE 1600W vacuum cleaners	25µm mesh size nylon sock	4 m² of bare floor for 4 minutes	Muenhor et al. (2017)
Not specified	Cellulose extraction thimble	Entire floor surface area of the room, accessible floor space under desks and tops of immovable furniture	Watkins et al. (2011)
Not specified	25µm mesh size nylon sock	Whole floor/elevated surface	Wu et al. (2016)
Philips FC6130, 900 W	Nylon filter bag	Not specified	Zhou et al. (2014)

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Chapitre 5. Halogenated flame retardants and organophosphate esters in the air of electronic waste recycling facilities: Evidence of high concentrations and multiple exposures.

Halogenated flame retardants and organophosphate esters in the air of electronic waste recycling facilities: Evidence of high concentrations and multiple exposures

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Cet article répond au troisième objectif de cette thèse. Il s’agit des résultats d’une évaluation de l’exposition professionnelle grâce à des prélèvements effectués sur le terrain. On y présente les niveaux d’exposition de travailleurs du recyclage électronique à des ignifuges de quatre classes chimiques, et les déterminants de l’exposition y sont identifiés.

Les analyses statistiques et la rédaction du manuscrit ont été effectuées par l’étudiante. La section analyse de laboratoire des ignifuges a été partiellement rédigée par des coauteurs (MD et LJ) et sa révision a également été effectuée par l’étudiante, jusqu’à sa publication. Le manuscrit a été révisé et approuvé par tous les coauteurs.

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5.1. Abstract

Background

In response to a worldwide increase in production of electronic waste, the e-recycling industry is growing. E-recycling workers are exposed to many potentially toxic contaminants, among which flame retardants (FRs), mainly suspected of being endocrine disruptors, are thought to be the most prevalent.

Objective

To conduct an exposure assessment of four chemical groups of FRs in Canadian e-recycling facilities, and to identify the main cofactors of exposure.

Methods

Personal air samples were collected over a workday for 85 workers in six e-recycling facilities, grouped into three facility sizes, and for 15 workers in control commercial waste facilities. Total particulate matter was measured by gravimetry with stationary air samples. FRs were collected on OSHA versatile samplers, which allow particulate and vapour phases collection. Fifteen polybrominated diphenyl ether congeners (PBDEs), nine novel brominated (NBFRs), two chlorinated (ClFRs), and fourteen organophosphate ester (OPEs) flame retardants were analyzed by gas chromatography-mass spectrometry. Sociodemographic data, tasks performed and materials processed by participating workers were recorded. Tobit regressions were used to identify cofactors of exposure, and their conclusions were corroborated using a semi-parametric reverse Cox regression.

Results

Thirty-nine of the 40 FRs analyzed were detected in at least one air sample in e-recycling, and workers in this industry were exposed on average to 26 (range 12 to 39) different substances. The most detected chemical group of FRs in e-recycling was PBDEs with a geometric mean sums of all congeners ranging from 120 to 5100 ng/m³, followed by OPEs with 740 to 1000 ng/m³, NBFRs with 7.6 to 100 ng/m³, and finally ClFRs with 3.9 to 32 mg/m³. The most important cofactor of exposure was the size of the e-recycling facility, with the largest one presenting on average 12 times the concentrations found in the control facility. Among tasks as potential cofactors of exposure, manual dismantling and baler operation exposed workers to some of the highest concentrations of PBDEs and ClFRs. There was a reduction of up to 27% in exposure to FRs associated with a 3 years increase in seniority. Finally, particulate matter concentrations in e-recycling facilities were highly correlated with all chemical groups except OPEs, and were higher in the large facility.

Conclusions

Among the FRs analyzed, PBDE exposure was particularly high in e-recycling. Dust and particulate matter reduction strategies in these workplaces, together with training on proper working practices would certainly be important first steps to lower occupational exposures and prevent potential health effects.

Keywords: E-waste; electronic recycling; polybrominated diphenyl ethers; organophosphate esters, flame retardants; occupational exposure; exposure assessment

5.2. Introduction

More than 44.7 million metric tonnes of electronic waste (e-waste) were generated worldwide in 2016, of which more than half originated from the Americas and Europe (Baldé et al. 2017). The increase in domestic consumption, as well as the perceived or functional obsolescence of technological equipment have contributed in recent decades to a substantial increase in production of e-waste (Premalatha et al. 2014). In response to a need for a responsible management of this hazardous waste, formal e-waste recycling (e-recycling) is a rapidly growing industry in higher income countries (Ceballos and Dong 2016; Déportes et al. 2018).

Despite its environmental advantages, e-recycling is not necessarily a "green" industry (Bakhiyi et al. 2018; Cheneval et al. 2016; Schulte et al. 2010). Numerous potentially toxic substances are found in e-waste, such as heavy metals and other elements, crystalline silica, plasticizers and flame retardants (FRs) (Ceballos et al. 2014). In order for electronics to meet flammability standards, FRs have been added to printed circuit boards, plastic casings and wire sheaths, among other components, since the 1970's (Besis and Samara 2012). The most commonly found FRs in older electronics are polybrominated diphenyl ethers (PBDEs), which were gradually superseded in newer electronics by less bioaccumulative, less environmentally persistent and presumably less toxic ones, such as novel brominated (NBFRs), chlorinated and organophosphate ester (OPEs) FRs (Abbasi et al. 2016; Harju et al. 2009; Webster and Stapleton 2012; Zhang et al. 2016).

Growing evidence shows that some FRs can have deleterious health effects. Indeed, non-occupational exposures to some PBDE congeners have been associated with thyroid and reproductive effects in the general population (Akutsu et al. 2008; Makey et al. 2016a). With the more recent chemical groups of FRs, endocrine effects are also suspected, as well as carcinogenicity, genotoxicity, and developmental neurotoxicity (Abou-Elwafa Abdallah 2016; EFSA Panel on Contaminants in the Food Chain (CONTAM) 2012; Li et al. 2013; Preston et al. 2017). Moreover, the concomitant exposure to these substances can have health implications that are still poorly understood (Crofton 2008; Curcic et al. 2014).

Workers in the e-recycling industry can be much more highly exposed to FRs than the general population. Some health effects such as DNA damage, hormonal disruption or adverse pregnancy outcomes have been noted in populations exposed to e-waste, but they were mostly observed in associations with exposure to informal e-recycling in low and middle income countries (Grant et al. 2013; Lu et al. 2017; Zheng et al. 2017). The primary treatment of e-waste, which consists of dismantling and crushing operations, increases the release of FRs into airborne dusts (Sun et al. 2016; Takigami et al. 2008), thereby exposing workers to those substances through inhalation, ingestion, and dermal exposure (Chen et al. 2019; Tsydenova and Bengtsson 2011). In formal e-recycling settings, two Swedish studies measured ambient concentrations of BDE209 ranging from 12 to 209 ng/m^3 in e-recycling facilities, compared to a maximum of 0.087 ng/m^3 in offices (Julander et al. 2005b; Sjodin et al. 2001). In China, Guo et al. (2015) measured BDE209 levels as high as 2170 ng/m^3 in the vicinity of plastic crushing operations. In a Finnish study that compared exposure to OPEs in different workplaces, geometric mean concentrations of triphenyl phosphate (TPhP) were up to 850 ng/m^3 in the breathing zone of e-recycling workers, which was at least 10 times higher than in a printed circuit board manufacturing plant, a furniture factory and an office building (Makinen et al. 2009). Furthermore, certain tasks in e-recycling, such as dismantling, have been shown to increase exposure to contaminants (Ceballos et al. 2017; Pettersson-Julander et al. 2004). By comparison, reported air FR concentrations vary greatly in informal e-recycling settings, with some studies reporting BDE209 levels as low as 0.27 ng/m^3 (Tue et al. 2013) and others measuring 417 ng/m^3 (An et al. 2011).

There is still a paucity of information regarding the exposure of formal e-recycling workers to the many potentially toxic FRs found in e-waste. So far, the only FR for which there is a recommended occupational exposure limit (OEL) is TPhP, with a threshold limit value (TLV®) of 3 mg/m^3 (American Conference of Governmental Industrial Hygienists 2019).

The goal of this article was to assess the exposure of workers to 40 flame retardants (FRs) from four chemical groups in six Canadian e-recycling facilities, as well as to identify important cofactors of exposure in order to guide future research and interventions in this industry.

5.3. Materials and methods

5.3.1. Study design

A cross-sectional study was conducted with the broad objectives to describe the e-recycling industry in terms of occupational health and safety practices, total airborne particulate matter (PM), metals and FR exposures by means of air sampling and biomarkers, and to assess endocrine effects of exposure. This article pertains specifically to personal air exposure data for FRs and total PM.

Six e-recycling facilities and one comparison facility were recruited, based on the following criteria: the e-recycling facility had to sort and dismantle electric or electronic equipment, with or without crushing or baling the resulting components, whereas the comparison recycling facility could recycle any material except electronics, and its operations had to include sorting and handling the materials. Recruited participants were asked to wear an air sampling pump over one workday. The tasks performed by participating workers and the materials handled on the sampling day were observed and recorded by a registered industrial hygienist (Canadian Registration Board of Occupational Hygienists). Workers were individually interviewed after the study to collect sociodemographic data (age, duration of employment in the facility, country of birth), various personal habits (smoking status, hand washing), and use of personal protective equipment.

The study was approved by the Université de Montréal health research ethics board, and the participants signed an informed consent form and received financial compensation. The directors of each facility also received an industrial hygiene assessment report.

5.3.2. Personal air samples and particulate matter collection

Sampling took place between May 2017 and March 2018. FRs were collected in the breathing zone of the workers using OSHA versatile samplers (OVS, SKC Ltd) containing a filter, XAD-2 sorbent, and a polyurethane foam plug which allowed for the collection of both the gas and particle phases of FRs. The breakthrough volumes of OVS tubes were calculated for 16 common flame retardants at 15°C (Supplementary material and supplementary Table S5.3).

OVSs were attached to high-flow Gilian GilAir-3 air sampling pumps (Sensidyne LP, St. Petersburg, FL) at a flow rate of 2 L/min for the whole work shift and were stopped during the workers' lunch time. The pump flows were calibrated with an air flow calibrator (Defender 510, Mesa Lab, NJ) before and after sampling, as well as upon restarting the pumps after lunch. The samples were transported on ice to the laboratory and stored at -20°C before extraction. One field blank was taken per facility, except in one large facility where three were taken. In each facility, three pre-weighted closed-face sampling cassettes (SKC, Eighty four, PA) were deployed for ambient sampling of total airborne PM at 2 L/min on 37 mm 0.8 μm pore size mixed cellulose ester filters (SKC, Eighty four, PA), for the entire workday. The three pumps were set in a generally busy area in the facilities.

5.3.3. Sample analysis

The target FRs and their abbreviations are listed in Table 5.1. The Chemical Abstract Service (CAS) registry number and molecular formula, as well as detailed methods for preparing OVS tubes, extraction and analytical procedures can be found in the Supplementary material (Tables S5.1 to S5.2). Briefly, OVS tubes were pre-cleaned using acetone: hexane:dichloromethane (Ace:Hex:DCM) in a 1:2:1 proportion, wrapped in aluminium foil, and stored in amber vials prior to sampling. Extraction of the OVS was performed with Ace:Hex:DCM, using a Supelco vacuum chamber (Bellefonte, PA, USA) after spiking with labelled surrogates for 5-10 minutes (Table S5.1).

Sample analysis was done with an Agilent 6890 Gas Chromatograph coupled with a 5975 Mass Selective Detector (GC-MS) using a DB-5 MS column (Agilent Technologies, 15 m x 0.25 mm i.d. x 0.25 μm film thickness). OPEs were analyzed in Electron Impact mode whereas PBDEs, NBFRs, dechloranes and tris(1,3-dichloro-2-propyl) phosphate (TDCiPP) were analyzed in electron capture negative ionization mode with methane as the reagent gas. OPE analyses were performed at the Environment and Climate Change Canada Centre for Atmospheric Research Experiments laboratory and extracts were transferred on ice to University of Toronto Earth Sciences laboratory for the analysis of PBDEs, NBFRs, dechloranes and TDCiPP.

Table 5.1. Identification of target flame retardants measured in personal air samples and percentage of values above the detection limit

Abbrev.	Name	% above LOD[a] Control (n=15)	E-recycling (n=88)
Polybrominated diphenyl ethers (n=15)			
BDE17	2,2',4-Tribromodiphenyl ether	0	2
BDE28	2,4,4'-Tribromodiphenyl ether	7	53
BDE47	2,2',4,4'-Tetrabromodiphenyl ether	100	100
BDE49	2,2',4,5'-Tetrabromodiphenyl ether	0	63
BDE66	2,3',4,4'-Tetrabromodiphenyl ether	13	81
BDE71	2,3',4',6-Tetrabromodiphenyl ether	0	34
BDE85	2,2',3,4,4'-Pentabromodiphenyl ether	0	49
BDE99	2,2',4,4',5-Pentabromodiphenyl ether	100	100
BDE100	2,2',4,4',6-Pentabromodiphenyl ether	7	34
BDE138	2,2',3,4,4',5'-Hexabromodiphenyl ether	0	17
BDE153	2,2',4,4',5,5'-Hexabromodiphenyl ether	13	88
BDE154	2,2',4,4',5,6'-Hexabromodiphenyl ether	0	75
BDE183	2,2',3,4,4',5',6-Heptabromodiphenyl ether	27	92
BDE190	2,2',3',4,4',5',6-Heptabromodiphenyl ether	33	56
BDE209	Decabromodiphenyl ether	73	100
Novel brominated (n=9)			
ATE	Allyl 2,4,6-tribromophenyl ether	53	72
DBDPE	Decabromodiphenylethane	0	58
HBB	Hexabromobenzene	0	69
OBIND	Octabromotrimethylphenyl indane	0	75
PBBz	Pentabromobenzene	7	64
PBEB	Pentabromoetheyl benzene	0	48
PBT	Pentabromotoluene	13	86
TBB	Ethylhexyl-tetrabromobenzoate	0	54
TBPH	Bis(2-ethlyhexyl) tetrabromophthalate	0	68
Chlorinated (n=2)			
s-DP	Dechlorane Plus (syn isomer)	73	100
a-DP	Dechlorane Plus (anti isomer)	80	100
Organophosphate esters (n=13)			
EHDPP	ethylhexyldiphenyl phosphate	100	98
TmCP	tris- meta cresyl phosphate	93	91
ToCP	tris- ortho cresyl phosphate	7	5
TpCP	tris- para cresyl phosphate	40	50
T2iPPP	tris(2-isopropyl phenyl) phosphate	20	64
TBOEP	tris-2-butoxyethyl-phosphate	33	89
TCEP	tris(2-chloroethyl) phosphate	67	100
TCiPP	tris(1-chloro-2-propyl) phosphate	100	90
TCPP2	bis(2-chloro-1-methylethyl) (2-chloropropyl) phosphate	67	53
TCPP3	Bis(2-chloropropyl) (2-Chloro-1-methylethyl) phosphate	7	1
TDCiPP	tris(1,3-dichloro-2-propyl) phosphate	100	100
TEHP	tris-2-ethylhexyl-phosphate	7	24
TnBP	tris-n-butyl phosphate	0	0
TPhP	tri-phenyl phosphate	100	100

[a] n=103: 15 control samples and 88 e-recycling samples

Abbrev., abbreviation; LOD, limit of detection

Field blanks consisted of OVS tubes brought to the field, taken out of the amber vial and aluminium foil at the time of fitting workers with their pumps, re-wrapped in aluminium and re-stored in the vial, then returned to the lab on ice along with the samples. Laboratory blanks were treated following the same procedure as the samples using only solvent and were analyzed with every batch of samples. There were a total of 15 procedural/lab blanks.

Total PM was measured by gravimetry. The filters were placed for at least 24h in a dessicator prior to being weighed in a controlled humidity chamber. The results presented consist of the mean concentration of the three ambient PM samples for all facilities, except in the large facility where six samples were taken over two visits.

5.3.4. Data analysis

Facilities and processes

The seven companies were grouped into three categories according to facility size and one control group. Differences between sizes in e-recycling facilities rested on the total number of employees in the facility assigned to e-recycling and on a qualitative assessment of the volume of e-waste processed. The large facility group included one facility, the medium facility group included two facilities and the small facility group comprised three facilities. The control group consisted in workers from the commercial waste recycling facility plus five workers from one of the small e-recycling facilities who were involved with paper products rather than recycling electronics.

Numerous tasks were recorded and were later categorized into five task groups, based on the similarity of tasks and the estimated overall exposure according to the hygienist's observations. The task groups were: "dismantling" (tasks involving manually disassembling the electronics), "manual handling" (handling of electronics except dismantling, i.e. sorting of incoming and outgoing goods and supplying a dismantling line), "baler operation" (feeding the baler with dismantled parts or whole electronics, compacting and removing the bales from the baler), "supervision" (supervising and managing workers in the facility, as well as office work), and "forklift operation" (transporting crates or bins using a forklift or a pallet truck).

Similarly, the materials predominantly handled or treated by the workers were classified as: "miscellaneous electronics" (whole electronic equipment other than televisions or computer screens, such as telephones, routers, speakers, etc.), "LCDs/LED/Plasma screens" (liquid crystal displays, light-emitting diode displays and plasma televisions or monitors), "Cathode ray tubes" (CRTs; televisions or monitors), "miscellaneous components" (dismantled components, such as batteries, wires, printed circuit boards, hard disks, etc.), and "none/general" (for workers who were in the facilities but did not manipulate any specific material). Also included in the information recorded were observations on the use of recommended personal protective equipment and frequency of hand washing during the workday.

The main task performed was determined to be the task executed by the worker for a majority (i.e. >50%) of the sampled day. If two tasks were performed for an equal time, the one that exposed workers the most to PM was selected, as determined by the industrial hygienist's judgement (e.g. dismantling against forklift operator). The same approach was used to identify the main material treated, where the material that was manipulated for the highest percentage of the day was selected.

Statistical analysis

In order to determine the correlation between the different FRs sampled in e-recycling facilities, Spearman's rank correlation coefficients were calculated between substances with at least 50% detection across air samples, where the values below the limit of detection were substituted with zero. The sum of all FR concentrations within chemical group was calculated per sample, and Spearman's rank correlation coefficients were computed between the geometric mean of those sums and the geometric mean concentrations of PM samples, per facility.

Univariate statistics were calculated per facility size group for 11 FRs, which were the three most detected FRs in e-recycling per chemical group. Arithmetic means, geometric means, geometric standard deviation, as well as their 95% confidence intervals (95% CIs), were calculated using the www.expostats.ca toolkit (Lavoue et al. 2019). This toolkit uses Bayesian statistics based on the assumption of a log normal distribution of exposures, which was adequate for our data as per quantile-quantile plots, allowing an optimal treatment of left-censored data (values below the limit of detection) (Huynh et al. 2016).

To identify important cofactors of exposure to the 11 FRs, a linear Tobit regression model was used (Lubin et al. 2004). With a left-censored dataset, while the coefficient can be in practice interpreted the same as a linear regression, the Tobit regression coefficient represents a combination of: 1) the probability of the FR concentration being detected, and 2) the change in the value of the FR concentration, if it is already above the detection limit, associated with the cofactor of interest (McDonald and Moffitt 1980). This method requires normality of the data and homoscedasticity to provide unbiased estimates (Holden 2004), and thus the regression was used on the natural log-transformed (for a better fit of the normal distribution) concentrations of the selected 11 FRs. To ensure a parsimonious model, covariables and confounders were identified a priori using a directed acyclic graph (Greenland et al. 1999). Hence, after verifying collinearity, two models were built to identify the important cofactors of exposure: the first contained the variables Task (categorical), adjusted on Gender (dichotomous), Duration of Employment (continuous, in 3-year increments), and Facility Size (categorical), and the second contained Materials Treated (categorical), adjusted on Facility Size.

To assess the robustness of the results, we used an alternative method that did not require prior assumptions on normality or homoscedasticity, namely a reverse-scale Cox regression model, as described by Dinse et al. (2014). Briefly, this method suggests the reversal of the exposure scale, by subtracting an arbitrary maximum value from every measured concentration, in order to obtain a right-censored distribution rather than left-censored. The reversed exposure scale is then used in a Cox regression model where it is treated as the outcome, under the proportional hazards assumption. This semi-parametric method yields a hazard ratio for each variable, which indicates the hazard of a category, such as a certain task, associated with higher exposures to a substance than the comparison category. The conclusions from both statistical approaches were compared, keeping in mind that the coefficients do not have the same meaning and can be compared only in terms of the direction of associations.

Statistical analyses were performed using STATA version 14.2 (StataCorp LLC, Texas).

5.4. Results

5.4.1. Facilities description

The e-recycling facilities differed in terms of their social mission (for profit or not), their size and production volume. The comparison facility recycled commercial waste which consisted mainly of glass, with a small volume of aluminium and cardboard. Sociodemographic characteristics of the recruited workers are presented in Table 5.2. It is noteworthy that only one facility had a respiratory protection program, that two had general ventilation, and that most workers were observed not to be adequately wearing their respiratory protection equipment, if wearing any. Overall, our sample consisted of 24 women and 77 men: 44 dismantlers (11 women), 17 manual handlers (6 women), 17 forklift operators (1 woman), 6 supervisors (2 women), 4 baler operators (all men) and 15 (4 women) controls. The 103 workers had a median duration of employment in the participating facilities of 2 years, ranging from 1 month to 22 years.

Table 5.2. Description of the participating facilities and workers

		Commercial recycling	**E-recycling**		
Facility size		**Control**	**Small**	**Medium**	**Large** [a]
Number recruited/Total employees in the facilities		15/21	22/24	30/57	36/65
Sex (M:F)		11:4	18:4	17:13	33:3
Age (median, range)		45, 24-69	49, 23-60	33, 21-57	41, 19-59
Current smoker		53%	23%	53%	19%
Duration of employment - months (median, range)		30, 3-180	42, 1-262	18, 1-108	21, 1-151
Born in Canada		100%	86%	90%	31%
Main task performed (n)	Supervision	-	2	1	3
	Forklift operator	5	4	5	8
	Manual handling	8	4	2	11
	Baler operator	2	0	1	3
	Dismantling	-	12	21	11
Material treated (n)	General/None	-	4	2	4
	Miscellaneous electronics	-	11	6	10
	LCDs/LED/Plasma screens[b]	-	1	8	5
	Miscellaneous components	-	5	6	7
	Cathode ray tubes	-	1	8	10

[a] Age, smoking status, duration of employment and country of birth are missing for two participants, and duration of employment is missing for one participant
[b] LCD: Liquid crystal displays; LED: light-emitting diode displays

5.4.2. Air flame retardant concentrations

A total of 103 personal air samples and 9 field blanks were collected. The mean sampling time was 456 minutes (over 7.5 hours) and varied between 112 and 664 min, corresponding to a mean collected air volume of 907 L (224 L – 1,310 L or 0.22 m^3 – 1.3 m^3, well below the theoretical breakthrough volumes). The percentage of samples above the LOD is presented in Table 5.1. Of the 40 FRs analyzed, 39 were detected in at least one sample in e-recycling, and 26 in the control group (Table 5.1). There was a high proportion of FRs that had > 30% censored values for NBFRs and for certain congeners of PBDEs in both types of recycling facilities. Interestingly, the proportion of values above the LOD for OPEs was similar in e-recycling and control groups, but the proportion was much higher in e-recycling for the other three chemical groups of FRs. In e-recycling facilities, all abundant PBDE congeners were highly correlated (all Spearman's ρ values > 0.75). Those PBDE congeners also correlated well with dechloranes, OBIND and TPhP (all $\rho > 0.71$). The Spearman's rank correlation coefficients for all substances detected in at least 50% of e-recycling samples are found in supplementary Table S5.4.

A profile of exposure to all substances by facility size group, in which the values below the limit of detection were replaced with zero, is presented in Figure 1. Overall, the control and the small facility size groups are exposed in greater proportion to OPEs, with the sum of OPEs representing 95% and 76% of the total exposure, respectively. Both tris(1-chloro-2-propyl) phosphate (TCiPP) and tris-2-butoxyethyl-phosphate (TBOEP) predominated in the control group, and TBOEP predominated in the small and medium size groups. The large facility size group was exposed to PBDEs in greater proportion (84% of total exposure), of which BDE209 was the main congener (99% of the sum of PBDEs). In this larger size group, the OPEs were dominated by TCiPP.

Univariate statistics by facility size are presented in Table 5.3 for the 11 selected FRs and for the sum of FRs per chemical group, as well as the detection frequencies of the major compounds detected. More detailed descriptive statistics, categorized by task and by material treated, are presented in supplementary Tables S5.5 and S5.6. E-recycling workers were exposed above the LOD on average to 26 (range 12-39) different FRs out of the 40 analyzed, and controls were exposed on average to 13 (range 7-20). The small facility size group was exposed above the LOD on average to 19 different FRs, the medium group to 25, and the large group to 31, and they were all exposed to the four chemical groups of FRs. The FR for which the highest concentration was measured in e-recycling was BDE209 in the large facility group, with a geometric mean of 5,100 ng/m³ and a maximum of 20,267 ng/m³. High concentrations of TPhP were also measured in the large facility, with a geometric mean of 220 ng/m³ and a maximum of 541 ng/m³. Some tasks or materials exposed workers to a greater number of substances. On average, 31 of the 40 FRs were detected for baler operators. The next greatest frequencies of detection were amongst manual handlers (27 FRs), dismantlers (26 FRs), forklift operators (25 FRs), supervisors (22 FRs), and finally controls (14 FRs). Handling CRTs exposed workers to more than 30 different FRs on average, followed by LCDs/LED/Plasma screens with 28 substances.

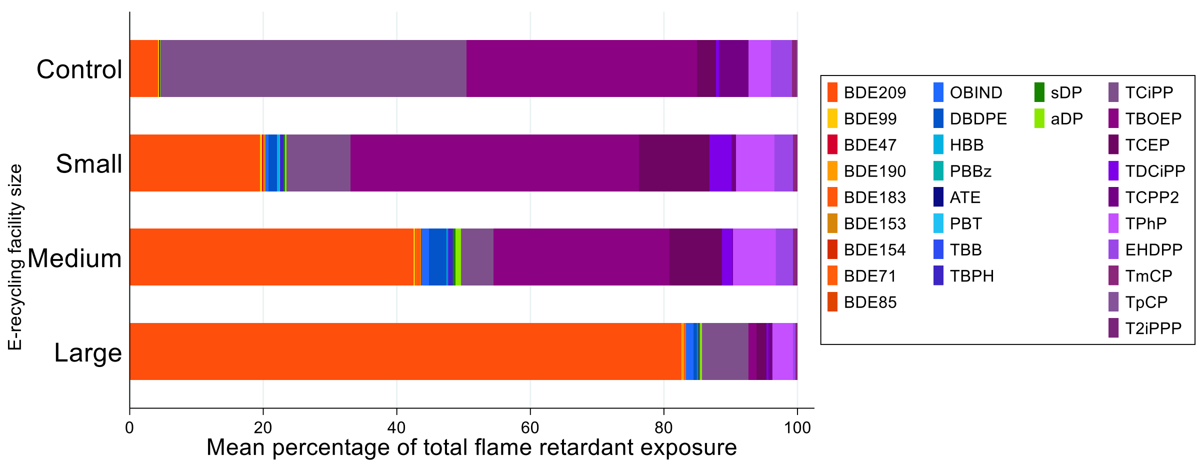

Figure 5.1. Contribution of each flame retardant to the total concentration of all flame retardants measured (ng/m³)

Table 5.3. Arithmetic and geometric mean concentrations of total particulate matter (mg/m³) and flame retardants (ng/m³) in the control and three facility size groups for selected flame retardants and for the sum by chemical group.

			Facility size		
		Control	**Small**	**Medium**	**Large**
Number of workers		15	22	30	36
Mean total PM (mg/m³)		7.9[b]	0.21[b]	0.78	1.8
	Number of PM samples	3	9	6	6
Mean n of FR detected		13/40	19/40	25/40	31/40
Polybrominated diphenyl ethers					
BDE47	**%>LOD**	100	100	100	100
	Mean [95% C.I.]	0.67 [0.44-1.2]	2 [1.5-3]	2.3 [2.1-2.7]	2.8 [2.4-3.5]
	GM [95% C.I.]	0.42 [0.28-0.64]	1.5 [1.1-2]	2.1 [1.9-2.4]	2.3 [1.9-2.7]
	GSD [95% C.I.]	2.6 [2.1-3.7]	2.2 [1.9-2.9]	1.5 [1.4-1.7]	1.9 [1.7-2.2]
BDE99	**%>LOD**	100	100	100	100
	Mean	0.95 [0.65-1.6]	3.6 [2.5-5.6]	3.8 [3.3-4.5]	5.5 [4.5-6.9]
	GM	0.65 [0.44-0.95]	2.3 [1.7-3.2]	3.4 [2.9-3.9]	4.3 [3.6-5.2]
	GSD	2.4 [1.9-3.3]	2.5 [2.1-3.3]	1.6 [1.5-1.8]	2 [1.8-2.3]
BDE209	**%>LOD**	73	100	100	100
	Mean	64 [23-460]	320 [170-830]	790 [630-1000]	6500 [5300-8400]
	GM	11 [4.6-25]	110 [64-180]	610 [500-760]	5100 [4100-6200]
	GSD	6.4 [3.9-15]	4.4 [3.2-6.8]	2 [1.8-2.4]	2 [1.8-2.4]
Mean n of congeners detected		4/15	6/15	9/15	12/15
ΣPBDE	**Mean**	88 [27-690]	320 [180-750]	810 [660-1100]	6600 [5400-8400]
	GM	10 [4.2-25]	120 [73-200]	640 [510-790]	5100 [4200-6200]
	GSD	7.9 [4.9-17]	4 [3-6.1]	2 [1.8-2.4]	2 [1.8-2.4]
Novel brominated flame retardants					
ATE	**%>LOD**	53	73	43	94
	Mean	0.16 [0.069-1.1]	0.29 [0.17-0.8]	0.45 [0.12-7.5]	0.49 [0.38-0.68]
	GM	0.041 [0.015-0.085]	0.11 [0.062-0.18]	0.022 [0.0067-0.05]	0.33 [0.25-0.42]
	GSD	5.3 [3.1-14]	4.1 [2.9-7.1]	12 [6-35]	2.4 [2.1-3]
OBIND	**%>LOD**	0	23	83	100
	Mean	-	22 [2.6-22000]	32 [19-70]	84 [69-110]
	GM	-	0.17 [0.010-0.79]	12 [7.7-18]	66 [54-80]
	GSD	-	23 [7.7-180]	4 [3.1-6.1]	2 [1.8-2.4]
PBT	**%>LOD**	13	50	97	100
	Mean	0.038 [0.0052-52]	0.37 [0.095-7.8]	0.34 [0.26-0.49]	0.51 [0.41-0.69]
	GM	0.00073 [1.2e-05-0.0052]	0.021 [0.0061-0.051]	0.23 [0.18-0.31]	0.37 [0.29-0.46]
	GSD	17 [5.2-200]	11 [5.6-35]	2.4 [2-3]	2.3 [2-2.7]
Mean n of NBFRs detected		1/9	3/9	7/9	7/9
ΣNBFR	**Mean**	0.2 [0.16-0.25]	98 [30-630]	85 [76-97]	150 [110-200]
	GM	0.18 [0.14-0.22]	7.6 [3.4-17]	79 [70-89]	100 [81-130]
	GSD	1.5 [1.3-1.9]	9.5 [6.1-18]	1.5 [1.4-1.6]	2.3 [2-2.8]
Chlorinated flame retardants					
aDP	**%>LOD**	80	100	67	100
	Mean	0.71 [0.35-2.6]	3.3 [2.3-5.4]	10 [7.3-15]	27 [22-34]
	GM	0.25 [0.12-0.47]	2.1 [1.5-3]	6.3 [4.7-8.4]	21 [17-26]
	GSD	4.3 [2.9-8.3]	2.6 [2.1-3.5]	2.6 [2.2-3.4]	2 [1.8-2.4]

		Control	Facility size		
			Small	Medium	Large
sDP	**%>LOD**	73	100	100	100
	Mean	0.36 [0.18-1.3]	3.1 [2-5.8]	6.3 [4.7-9.3]	14 [12-18]
	GM	0.13 [0.062-0.24]	1.7 [1.1-2.5]	4.1 [3.1-5.5]	11 [8.9-13]
	GSD	4.2 [2.8-8.2]	3.1 [2.5-4.3]	2.5 [2.1-3.2]	2.1 [1.8-2.5]
Mean n of ClFRs detected		2/2	2/2	2/2	2/2
ΣDP	**Mean**	1.2 [0.54-5.7]	6.5 [4.4-11]	16 [12-24]	41 [34-53]
	GM	0.33 [0.15-0.67]	3.9 [2.7-5.5]	11 [7.9-14]	32 [26-39]
	GSD	5.1 [3.3-10]	2.8 [2.2-3.7]	2.6 [2.2-3.2]	2 [1.8-2.4]
Organophosphate esters					
TCEP	**%>LOD**	67	100	100	100
	Mean	950 [53-6E^5]	130 [110-160]	140 [130-160]	120 [100-130]
	GM	2.4 [0.42-11]	110 [90-130]	130 [120-150]	110 [97-120]
	GSD	32 [12-150]	1.7 [1.5-2]	1.5 [1.4-1.6]	1.5 [1.4-1.6]
TDCiPP	**%>LOD**	100	100	100	100
	Mean	4.5 [3.4-6.5]	20 [12-42]	30 [25-36]	24 [20-29]
	GM	3.6 [2.7-4.8]	9.3 [5.9-15]	25 [21-30]	20 [17-24]
	GSD	1.9 [1.6-2.5]	3.5 [2.7-5.1]	1.7 [1.6-2]	1.8 [1.7-2.1]
TPhP	**%>LOD**	100	100	100	100
	Mean	32 [24-47]	72 [53-110]	120 [100-140]	240 [210-280]
	GM	25 [19-34]	50 [37-68]	100 [88-120]	220 [190-250]
	GSD	2 [1.7-2.6]	2.4 [2-3.1]	1.7 [1.5-2]	1.6 [1.5-1.8]
Mean n of OPEs detected		7/14	8/14	8/14	10/14
ΣOPEs	**Mean**	920 [660-1400]	980 [750-1400]	900 [770-1100]	1100 [980-1300]
	GM	680 [490-960]	740 [570-970]	780 [660-920]	1000 [890-1100]
	GSD	2.2 [1.8-2.9]	2.1 [1.8-2.7]	1.7 [1.6-2]	1.5 [1.4-1.7]

[a] The 3 FRs per chemical group with the highest detection proportion, and a higher exposure in e-recycling than in the control group

[b] Total particulate matter (PM) for Control group are only available for facility D, and total PM for Low group comprises 5 workers of facility F.

5.4.3. Total particulate matter

In all of the facilities, the PM concentrations were below the TLV® of 10 mg/m^3 for inhalable particulate matter (American Conference of Governmental Industrial Hygienists 2019). The PM concentrations in the control facility were higher than in e-recycling, but the FR concentrations were much lower. Among the e-recycling facilities, the mean PM concentration in the large one was significantly higher than in the small facility group (mean difference of 1.6 mg/m^3, 95% CI: [-2.7 – -.47]). Total PM concentrations in e-recycling facilities were highly correlated with the geometric mean sum of PBDE congeners (Spearman's ρ=0.77, p=0.072), with NBFRs (ρ=0.89, p=0.019) and dechloranes (ρ=0.94, p=0.005), but not with OPEs (ρ=0.26, 0.62).

5.4.4. Important cofactors of exposure

For the 11 FRs described, the Tobit regression coefficients and their 95% CIs for the different tasks (in models adjusted for gender, seniority and facility size) or material treated (in models adjusted for facility size), are presented in Figure 5.2 (detailed results in Table S5.7). In these multivariable analyses, a significant reduction of 27% in mean PBT, of 13% in TPhP, and of up to 20% in mean PBDE exposure were associated with a 3-year increase in experience duration. Gender was not an important cofactor of exposure to FRs, although women tended to have lower exposures to some FRs than men (from 7% to 32% lower in BDE209, OBIND, both dechloranes and all OPEs). The main covariate that was associated with higher exposures to almost all FRs was the facility size, with an average 3-fold increase in concentrations in the medium facility group, and an average 12-fold increase in the large facility group, compared to the control group. Among tasks, dismantling was significantly associated with concentrations of aDP (exponentiated beta [e^{β}] = 4.6, 95% CI = 2.5–8.5) and sDP (e^{β} = 5.8, 95% CI = 3.1–1.8) four to five times higher than the reference task (supervision), and between one and two times higher for TDCiPP (e^{β} = 2.7, 95% CI = 1.4–4.9) and TCEP (e^{β} = 1.6, 95% CI = 1.2–2.3). Baler operation was also associated with higher exposures to all substances except ATE, although not always reaching statistical significance most likely because of a small sample size (e^{β}s ranging from 1.4 to 3.5). All tasks were significantly associated with higher PBDE (e^{β}s from 1.9 to 3.6) and dechloranes (e^{β}s from 2.8 to 5.8) concentrations than the reference task (supervision), but not with NBFR concentrations, and dismantling only with OPEs (e^{β}s from 1.6 to 2.7). Cathode ray tube TVs and LCD/LED/Plasma screens (TVs and monitors) were the two materials most associated with increased exposures to all FRs (e^{β}s up to 2.8 and 6.4 for sDP exposure, respectively), except for ATE.

The conclusions drawn from the reverse Cox regression were similar to those drawn from the Tobit regressions and the signs of the significant coefficients were identical. Both approaches identified baler operating and dismantling tasks to be associated with higher exposures, and the facility size to be an important cofactor of exposure as well. The results of the reverse Cox regressions are presented in Table S5.8.

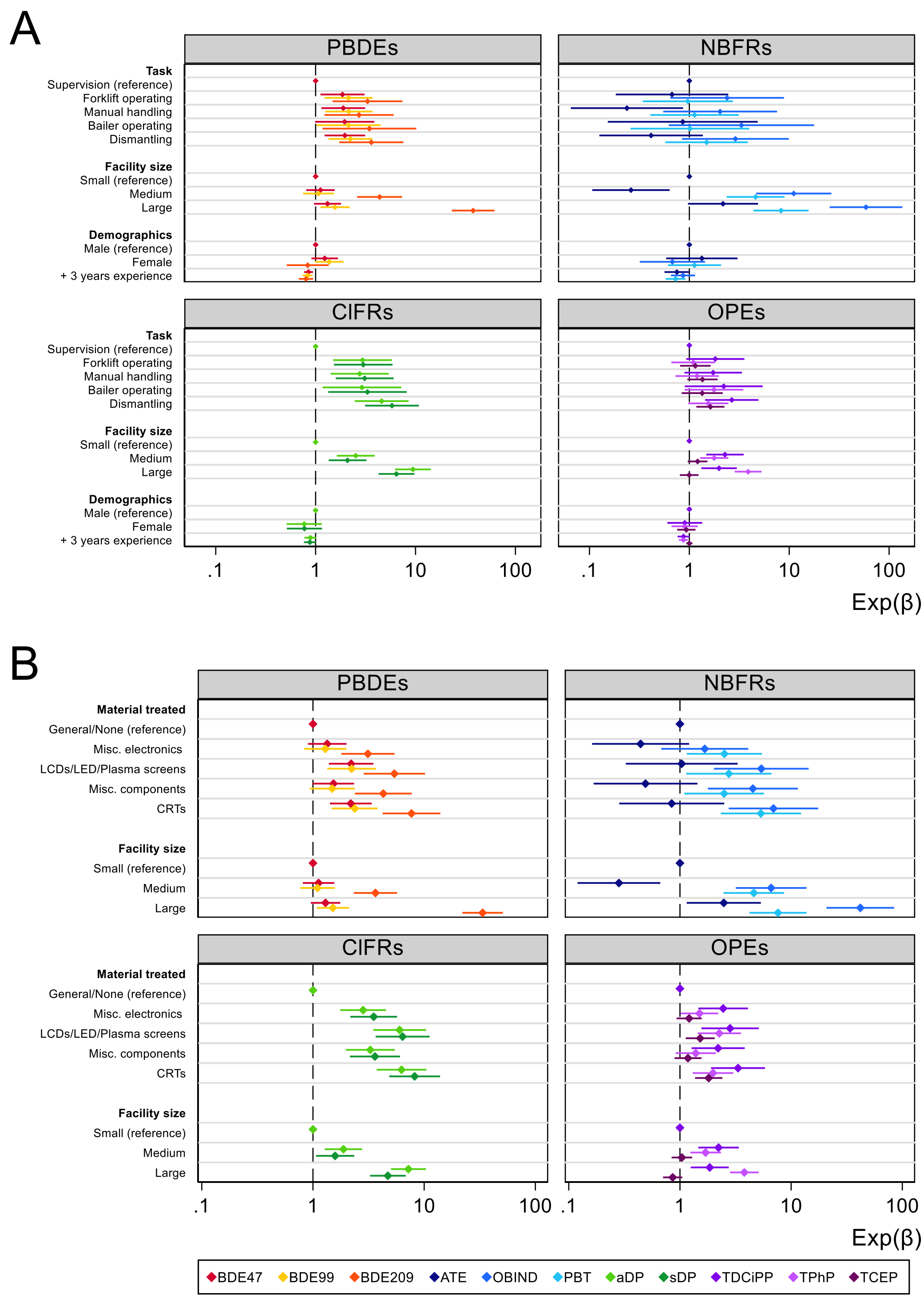

Figure 5.2. Association of cofactors with flame retardant concentration in the electronic recycling facilities.

The exponentiated Tobit regression coefficients and their 95% confidence intervals are represented for 11 flame retardants. Model A presents the effect of task, facility size and demographic variables, and Model B presents the effect of materials treated and facility size. Dashed line at x=1 represents the reference, meaning no effect.

5.5. Discussion

Our study is the first occupational exposure assessment in formal e-recycling facilities to report exposure to four chemical groups of flame retardants using personal air monitoring. It sheds light on the multiple potentially toxic and bioaccumulative substances to which e-recycling workers may be exposed (EFSA Panel on Contaminants in the Food Chain (CONTAM) 2012; Harju et al. 2009), and identifies tasks and materials that were found to be associated with higher concentrations of FRs.

The most abundant FR found in the air of e-recycling facilities was by far BDE209. This PBDE congener is the main component of the phased-out DecaBDE commercial formulation, which has been restricted and banned in Canada (Government of Canada 2016) and in the European Union, and is voluntarily phased-out or restricted for new uses in many states in the US ("Deca-BDE to be phased-out" 2010; Dodson et al. 2017; Jinhui et al. 2017). The Canadian regulation pertains only to new uses of PBDEs and does not cover their use in finished goods manufactured or imported before January 1, 2017. As mentioned by Abbasi et al. (2015), it will hence take years for currently used products containing DecaBDEs to move through the waste stream and be finally discarded. Air concentrations of BDE209 were particularly high in the breathing zone of workers manipulating cathode ray tube TVs and monitors, but also newer types of devices such as LCDs, LED, and plasma screens. CRTs can indeed contain from 5 to 400 times higher DecaBDE concentrations than other electronic equipment (Abbasi et al. 2015). TPhP and TCEP concentrations were the highest in e-recycling among all OPEs analyzed, and they were associated with both types of TV monitors as well. This indicates that although the quantity of recycled CRTs has diminished since its peak in 2005 (Abbasi et al. 2015; Singh et al. 2016), e-recycling workers are still exposed to a cocktail of old and newer flame retardants, and it may remain this way for years to come.

Two studies in formal e-recycling facilities reported BDE209 concentrations using personal air sampling: one held in 2000 in Sweden where the highest mean was 30 ng/m³ (Pettersson-Julander et al. 2004), and one in Finland in 2008 and 2009 where the highest mean concentration was 2002 ng/m³ (Rosenberg et al. 2011). Our highest mean of 6500 ng/m³ in BDE209 is much higher than those reports, which may raise some concern about potential health effects of such high exposures. On the other hand, the geometric mean level of TPhP that we measured (94.3 ng/m³ for all e-recycling facilities) was about nine times lower than the level reported in another Finnish study (850 ng/m³, ambient air sampling) (Makinen et al. 2009). In comparison, median TPhP values ranging from 5.0 to 5.7 ng/m³ were measured with stationary passive air samplers in Canadian homes (Okeme et al. 2018; Yang et al. 2019).

We have shown that the relative proportion of exposure to the different FRs found in e-recycling or in the control group differ from one another, where controls were exposed to a greater relative proportion of OPEs, and e-recyclers were exposed to a greater proportion of PBDEs, increasing with the size of the facility. The large facility group was observed to have a greater volume of CRTs to recycle (data not recorded) than the other facility groups, which can explain the relative proportions of FRs, as well as higher concentrations, especially of BDE-209, OBIND and DPDPE that have been found in TVs (Abbasi et al. 2016). The relative proportions that we calculated was different from the ones found by Sjodin et al. (2001), who did not observe a predominance of PBDEs, perhaps because the facility that they sampled corresponded more to one of our small or medium facilities. There is also a close to 20-year gap between these European studies and ours, which can in part explain the different flame retardant exposure patterns and concentrations observed in e-waste recycling across those different countries.

Our results are consistent with those of Pettersson-Julander et al. (2004) who found that e-waste dismantlers were generally more exposed to contaminants than workers performing less destructive tasks such as sorting, shipping and receiving (included in our "manual handling" group). Baler operation was the task associated with the highest number and with some of the highest concentrations of FRs. Baling requires the operator to fill the baler, to mechanically crush the contents, and to repeat the process until a bale of a certain size is produced, which generates a lot of PM. In one small facility, plastic computer parts were mechanically shredded, and the worker who operated this machine for approximately 10 minutes ended up with the highest measured level of BDE99 and the fifth highest of BDE47. Hence, PM-generating processes in e-recycling such as shredding and baling can be important sources of airborne FRs. E-recycling tasks were significantly associated with exposures to PBDEs, dechloranes and OPEs, but not with NBFRs. The latter presented the most variability among the different tasks (geometric standard deviation up to 9.1 for OBIND exposure in dismantlers), which may explain the poor associations observed. In our study, the size of the e-recycling facility seemed to be the most influential cofactor of exposure. In the medium and the large facilities, workers were required to work at a faster pace than in the small facilities in order to process a larger volume of materials. This had a visible impact on their working methods: they were observed to favor the use of hammers rather than screwdrivers to dismantle large equipments, or to throw components rather than deposit them into boxes, which visibly produced more PM. Training on adequate work practices could be another interesting exposure prevention approach.

We found that the total PM concentrations in e-recycling facilities were correlated with total airborne FR concentrations of PBDEs, NBFRs and dechloranes, a finding consistent with these compounds being often particle-sorbed (Takigami et al. 2008). The correlation between PM and FRs suggests that focusing on PM monitoring and reduction could be an efficient way to reduce exposure to FRs in e-recycling facilities. A general occupational hygiene remediation approach would be to implement better ventilation and perhaps aspiration near worktables and dust-generating machinery in order to reduce PM levels. Such measures were shown to yield a 10-68% reduction in personal exposure to FRs in Finnish e-recycling facilities (Rosenberg et al. 2011). The PM concentration in the control facility was higher than in e-recycling, but considering the materials processed, it was suspected of consisting mainly of paper/cardboard fibers (bottle labels and boxes), amorphous silica and bioaerosols (Poulsen et al. 1995).

In the absence of occupational threshold limit values, it is difficult to determine if the air concentrations measured can present a risk for workers' health. A maximum allowable concentration of 0.7 mg/m³ for PentaBDE was proposed by the Polish Central Institute for Labor Protection in 2012 (Szymańska and Bruchajzer 2012), but has never been implemented. The highest TPhP value that we recorded represents 0.02% of the 3 mg/m³ TLV®. However, this recommended occupational limit was never revised since it was established in 2001 based on 1992 documentation of eye and skin irritation and cholinesterase inhibition. As such, this TLV® is not necessarily protective for other more recently suspected health effects in workers (American Conference of Governmental Industrial Hygienists 2001).

There are some limitations to this study. Our samples were obtained in six different e-recycling facilities in the Canadian province of Québec, and may not necessarily be representative of the whole industrial sector. The workers were observed to move within the facility and were assigned varying tasks throughout the day in most facilities, which complicated the classification of tasks and of material treated. Misclassification and some uncertainty in exposure levels measured in each group is thus inevitable. Finally, considering the workers' movements throughout their day, stationary sampling at the worktables in addition to personal air sampling could have improved the identification of task-specific exposures.

Our study has several strengths, of which the greatest remain the wide array of contaminants tested, the duration of sampling that spanned over a complete work shift, and the air sampling in the breathing zone of workers. As well, we identified a few main cofactors of exposure to FRs. In addition, the diversity of the formal e-recycling facilities visited and the number of whole work shift samples acquired are unprecedented. We also explored a few approaches in the statistical treatment of censored FR data by corroborating our results using a semi-parametric statistical method that could accommodate for heteroscedasticity and a high proportion of censored data.

5.6. Conclusion

Formal recycling of electrical and electronic equipment is thought to be a more efficient and environmentally-sound way of dealing with an increasing quantity of e-waste, as opposed to dumping in landfills. As this industry is growing to meet the annual increase of e-waste, it is important to identify occupational hazards that can arise in order to control them before health effects appear. Among the four chemical groups of FRs analyzed in our study, DecaBDE exposure was particularly high, but we can expect the proportion of OPEs, which are thought to have replaced now-banned PBDEs, to increase in the coming decades as newer electronics attain their end-of-life. Workers operating dust-generating machinery, as well as those manipulating CRT TVs are more likely to undergo higher exposures to flame retardants than other workers. Dust reduction in these workplaces would certainly be an important first preventive step.

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The authors have no conflict of interest to declare.

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5.8. Supplementary material

5.8.1. Sample analysis

Chemicals and supplies

All chemicals are listed in Table1. For organophosphate esters (OPEs), a certified mix was purchased from AccuStandard Inc (New Haven, CT, USA), chlorinated and all brominated flame retardants were purchased from Wellington Laboratories Inc. (Guelph, Ontario, Canada). All glassware and vials were washed with soap and water, rinsed with acetone and baked overnight at 400°C. Aluminum foil was cleaned by baking at 400°C. All solvents were High-Performance Liquid Chromatography, spectrometry and/or gas chromatography grade. Acetone, dichloromethane, hexanes, methanol and 2,2,4-Trimethylpentane (Isooctane) (VWR OmniSolv®), nitrogen and helium were grade 5.0 99.999% (Linde), and methane was the highest grade (99.95%). Extraction solution consisted of acetone: hexane:dichloromethane (Ace:Hex:DCM) in a 1:2:1 proportion, prepared by a laboratory technician.

Preparation of OSHA Versatile Samplers (OVS)

OVSs consist of a glass tube containing a glass fiber filter to collect particles and a sandwich of polyurethane foam and XAD-2 resin (hydrophobic copolymer of styrene-divinylbenzene) for adsorption of vapour phase compounds (OVS; SKC Ltd, Eighty Four, PA, USA). OVS samplers were cleaned with methanol followed by a mixture of Ace:Hex:DCM, dried with nitrogen then wrapped in aluminium foil and kept in amber glass vials (VWR) at room temperature until use.

Extraction

The gas and particle phases were not separated for analysis. Extraction of the OVS tubes is done using a Supelco vacuum chamber (Bellefonte, PA, USA). The vacuum chamber was prepared by sonicating the needles in methanol and the glass chamber was rinsed with methanol. OVS tubes were spiked with a mixture of labelled surrogates (Table S5.1) to assess extraction efficiencies. The surrogates were left to absorb to the tubes for 5-10 minutes followed by extraction with 15 mL of the Ace:Hex:DCM mixture. Samples were reduced to 0.5 ml with a gentle stream of nitrogen. Internal standards for volume correction and time reference (Mirex for the OPEs and BDE-118 and BDE-181 for HFRs) were added prior to analysis.

Instrument and analysis

Sample analysis for OPEs (except TDCiPP) was done on an Agilent 6890 Gas Chromatograph (GC) coupled with a 5975 Mass Selective Detector (MSD), operating in Electron Impact (EI) mode. Two µL pulsed split-splitless injection were done on an Equity (Supelco) or DB-5MS capillary column (30-m x 0.25mm diameter x 0.25 µm film thickness; Bellefonte, PA, USA).The temperature program was as follows: initial 90°C held for 1 min, a ramp at 20°C/min up to 160°C, a ramp at 5°C/min up to 250, a final ramp at 20°C/min up to 310°C that was held for 5 min. Carrier gas (helium) flow rate was 1.2 mL/min. Other parameters were: injector 200°C, transfer line at 280°C, source 230°C and quadrupole 150°C. BFRs, ClFRs and TDiCPP were analyzed using a DB-5 MS column (Agilent Technologies, 15 m x 0.25 mm i.d. x 0.25 µm film thickness) operating in electron capture negative ionization mode with methane as the regent gas with the following oven temperature program: initial at 100°C hold for 1.5 min, 12°C/min to 250°C, then 6°C/min to 290°C, hold for 3 min, and 60°C/min to 320°C, hold for 12 min. Post run at 310 °C for 2 min. Injection volume was 2 µL at splitless mode with inlet temperature of 275 °C. Helium carrier gas flow rate was 1.5 mL/min. Full scans of all individual compounds were performed to determine target and qualifier ions, see Table S5.2. OPEs analyses were performed at Environment and Climate Change Canada lab and samples were transferred on ice to University of Toronto laboratory for the remainder of the target compounds, see Table 5.1.

QA/QC

Breakthrough volume of an OVS tube was the sum of breakthrough volume of polyurethane foam and XAD -2 for 16 common flame retardants at 15°C (Table S5.3). The mass of XAD-2 in an OVS tube is 0.27g, the mass of PUF is 0.04g, and the density of XAD-2 is 640 kg/m^3.

Breakthrough volume of PUF was estimated by using Equation 12 (Hayward et al. 2011) and Abraham solvation parameters used in a polyparameter linear free energy relationship (pp-LFER) for flame retardants (Center for Environmental Research – UFZ 2018). Breakthrough volume of XAD-2 was estimated by using Equation 4, 9 and 13 (Hayward et al., 2011). The smallest breakthrough volume of OVS at 15°C (40 m^3) was for tris(2-chloroethyl)phosphate (TCEP). The air volumes collected through OVS tubes in this study (average sampling volume of 0.89m^3) were much lower than the estimated breakthrough volume.

The target/qualifier ion ratio must be within ±20% of the standards to ensure peak purity. To assess analyte recovery and efficiency of the method, all samples were spiked with a surrogate standard containing isotopically labelled OPEs and BFRs. Surrogate standard recoveries and matrix spike recoveries were considered satisfactory if they were between 50 – 150 %, and were corrected if they were below 50% (Table S5.1). Recoveries of $^{13}C_{18}$TPhP and d_{12}TCEP were on average higher than 100% and were higher than the recovery of the surrogates in the blanks. This could be due to sample matrix effects or ion bleed from the native compound (Stubbings et al. 2019). Recoveries of the surrogates for the samples and blanks were acceptable so the samples were not recovery corrected.

The method detection limit (MDL) of each of the target compounds was defined as the average field blank plus three times the standard deviation of the blanks. When no detection for a compound was found in the blanks, the MDL was defined as the instrumental limit of detection (LOD). The LODs were derived from an extrapolated signal to noise ratio of 10:1 of the standard calibration curve for BFRs, ClFRs , and TDCiPP. They were defined as the lowest standard injected for OPEs (i.e. 0.1-5 pg/uL depending on the compound, see Table 5.1. Blank results were considered using the following criteria: samples were not blank-corrected if the MDL was < 10% of total sample concentration; blank-corrected using the average blank concentration if the MDL was between 10% - 35% of sample concentration; and rejected if the MDL> 35% of sample concentration. The two laboratories that performed the analyses participated in an inter-lab calibrations exercise (Melymuk et al. 2015).

Table S5.1. Labelled surrogates, target ions and recovery ranges, and relative standard deviation

		Recovery	
Surrogate	Ion target	Range (%)	Relative standard deviation (%)
$^{13}C_6$-PBBz	479.7	68-112	9.7
D_{15}-TDCiPP	332	59-114	13
$^{13}C_6$-HBB	561.5	68-111	11
F-BDE-100	501	69-116	9.5
F-BDE-154	81	71-106	7.9
F-BDE-208	488.5	48-103[a]	14
d_{27}-TnBP	103	48-126[b]	17
d_{12}-TCEP	261	61-212	24
$^{13}C_{18}$-TPhP	344	50-176	26

[a] The minimum value of 48 was in a solvent blank sample and therefore no correction was applied.
[b] All samples were below the limit of detection, therefore no correction was applied

Table S5.2. Ions of the target compounds

Abbreviation	CAS No.	Molecular formula	Detection limit[a] (ng/m³)	Target ion	Qualifiers Ion 1	Ion 2	Ion 3
Polybrominated diphenyl ethers (ECNI mode)							
BDE17	147217-75-2	$C_{13}H_9Br_3O_2$	0.031	78.9	80.9		
BDE28	41318-75-6	$C_{12}H_7Br_3O$	0.031	78.9	80.9		
BDE47	5436-43-1	$C_{12}H_6Br_4O$	0.031	78.9	80.9		
BDE49	243982-82-3	$C_{12}H_6Br_4O$	0.031	78.9	80.9		
BDE66	189084-61-5	$C_{12}H_6Br_4O$	0.031	80.9	78.9		
BDE71	189084-62-6	$C_{12}H_6Br_4O$	0.031	78.9	80.9		
BDE85	182346-21-0	$C_{12}H_5Br_5O$	0.031	78.9	80.9		
BDE99	60348-60-9	$C_{12}H_5Br_5O$	0.031	78.9	80.9		
BDE100	189084-64-8	$C_{12}H_5Br_5O$	0.031	80.9	78.9	402.9	
BDE138	182677-30-1	$C_{12}H_4Br_6O$	0.041	80.9	78.9		
BDE153	68631-49-2	$C_{12}H_4Br_6O$	0.041	78.9	80.9	403.6	562.6
BDE154	207122-15-4	$C_{12}H_4Br_6O$	0.031	78.9	80.9	483.7	563.7
BDE183	207122-16-5	$C_{12}H_3Br_7O$	0.041	80.9	78.9	483.6	561.6
BDE190	189084-68-2	$C_{12}H_3Br_7O$	0.010	78.9	80.9		
BDE209	1163-19-5	$C_{12}Br_{10}O$	2.6	488.8	80.9	78.9	
Novel brominated (ECNI mode)							
ATE	3278-89-5	$C_9H_7Br_3O$	0.020	78.9	80.9	290.8	
DBDPE	84852-53-9	$C_{14}H_4Br_{10}$	1.2	80.9	78.9		
HBB	87-82-1	C_6Br_6	0.0051	549.5	469.7	471.6	
OBIND	1084889-51-9	$C_{18}H_{12}Br_8$	1.0	78.9	80.9		
PBBz	608-90-2	C_6HBr_5	0.0051	471.7	469.7	393.7	
PBEB	85-22-3	$C_8H_5Br_5$	0.010	78.9	80.9	501.8	499.8
PBT	87-83-2	$C_7H_3Br_5$	0.010	78.9	80.9	485.7	487.7
TBB	26040-51-7	$C_{15}H_{19}Br_4O_2$	0.20	78.9	80.9	356.8	358.7
TBPH	26040-51-7	$C_{24}H_{34}Br_4O_4$	0.51	78.9	383.6	514.6	
Chlorinated (ECNI mode)							
s-DP	13560-89-9	$C_{18}H_{12}Cl_{12}$	0.051	651.8	653.8	655.8	
a-DP	13560-89-9	$C_{18}H_{12}Cl_{12}$	0.051	653.8	651.8	655.8	
Organophosphate esters (EI mode except TDCiPP)							
EHDPP	1241-94-7	$C_{20}H_{27}O_4P$	0.051	251	250		
TmCP	1330-78-5	$C_{21}H_{21}O_4P$	0.010	368	367		
ToCP	1330-78-5	$C_{21}H_{21}O_4P$	0.010	368	367		
TpCP	1330-78-5	$C_{21}H_{21}O_4P$	0.010	368	367		
T2iPPP	64532-95-2	$C_{27}H_{33}O_4P$	0.051	118	452		
TBOEP	78-51-3	$C_{18}H_{39}O_7P$	0.51	57	85		
TCEP	115-96-8	$C_6H_{12}Cl_3O_4P$	0.10	249	251		
TCiPP	13674-84-5	$C_9H_{18}Cl_3O_4P$	0.051	99	125		
TCPP2	76025-08-6	$C_9H_{18}Cl_3O_4P$	0.051	99	125		
TCPP3	76649-15-5	$C_9H_{18}C_{l3}O_4P$	0.051	99	125		
TDCiPP	13674-87-8	$C_9H_{15}Cl_6O_4P$	0.051	317	319		
TEHP	78-42-2	$C_{24}H_{51}O_4P$	0.10	99	113		
TnBP	126-73-8	$C_{12}H_{27}O_4P$	0.051	99	57		
TPhP	115-86-6	$C_{18}H_{15}O_4P$	0.051	326	325		

[a] Average sampling volume of 0.907 m^3

Table S5.3. Estimated breakthrough volumes of an OSHA versatile sampler (OVS) tube at 15 °C for 16 common flame retardants.

	Estimated breakthrough volume (m^3)
Polybrominated diphenyl ethers	
BDE28	263
BDE47	1530
BDE99	46020
BDE100	6480
BDE153	257000
BDE154	44600
Organophosphorus esters	
EHDPP	196000
TmCP	224000
ToCP	224000
TpCP	224000
TBOEP	185000
TCEP	40
TCiPP/TCPP2/TCPP3	105
TDCiPP	6670
TEHP	2770000
TPhP	2690

[a] See section 5 QA/QC (page 3) for a description of the method of estimation

Table S5.4. Spearman's rank correlation between flame retardants that had at least 50% detection, in e-recycling 2017-2018

	Polybrominated diphenyl ethers (PBDEs)										Novel brominated flame retardants (NBFRs)								Chlorinated flame retardants (ClFRs)		Organophosphate esters (OPEs)								
	BDE28	BDE47	BDE49	BDE66	BDE99	BDE153	BDE154	BDE183	BDE190	BDE209	ATE	OBIND	PBBz	HBB	PBT	TBPH	TBB	DBDPE	aDP	sDP	TCEP	TDCiPP	TPhP	TCPP2	EHDPP	TBOEP	TmCP	TpCP	T2iPPP
BDE28	1																												
BDE47	.64*	1																											
BDE49	.58*	.56	1																										
BDE66	.71*	.63*	.46*	1																									
BDE99	.66*	.96*	.65*	.62*	1																								
BDE153	.50*	.49*	.83*	.40*	.58*	1																							
BDE154	.59*	.58*	.76*	.56*	.65*	.79*	1																						
BDE183	.52*	.48*	.81*	.45*	.56*	.90*	.88*	1																					
BDE190	.48*	.40*	.83*	.36*	.50*	.81*	.75*	.87*	1																				
BDE209	.55*	.46*	.83*	.50*	.53*	.85*	.79*	.86*	.89*	1																			
ATE	.39*	.33*	.49*	.26*	.40*	.48*	.41*	.43*	.58*	.51*	1																		
OBIND	.59*	.44*	.76*	.51*	.53*	.77*	.79*	.82*	.82*	.94*	.51*	1																	
PBBz	.45*	.37*	.70*	.40*	.41*	.69*	.62*	.69*	.74*	.81*	.51*	.76*	1																
HBB	.46*	.32*	.56*	.43*	.33*	.57*	.52*	.57*	.65*	.76*	.36*	.74*	.81*	1															
PBT	.54*	.47*	.60*	.60*	.52*	.57*	.60*	.61*	.52*	.73*	.40*	.73*	.63*	.64*	1														
TBPH	.14	.13	.20	.16	.17	.31*	.39*	.36*	.13	.20	-.07	.19	.10	.04	.10	1													
TBB	.14	.23*	.03	.25*	.22*	.08	.25*	.16	-.13	.00	-.21*	.03	-.09	-.06	.22*	.56*	1												
DBDPE	.18	.45*	.23*	.35*	.43*	.22*	.33*	.27*	.04*	.18	.01	.17	.19	.10	.33*	.30*	.52*	1											
aDP	.61*	.49*	.77*	.52*	.57*	.84*	.84*	.89*	.85*	.92*	.51*	.91*	.76*	.70*	.70*	.31*	.14	.20	1										
sDP	.63*	.48*	.71*	.55*	.56*	.79*	.75*	.80*	.74*	.86*	.43*	.89*	.72*	.71*	.67*	.35*	.16	.24*	.94*	1									
TCEP	.32*	.31*	.17	.33*	.34*	.21*	.25*	.15	-.02	.10*	.14	.12	.03	.05	.30*	.34*	.49*	.36*	.19	.26*	1								
TDCiPP	.50*	.43*	.40*	.56*	.47*	.44*	.64*	.56*	.31*	.42*	.09	.49*	.27*	.23*	.48*	.57*	.62*	.47*	.55*	.59*	.48*	1							
TPhP	.54*	.54*	.76*	.51*	.62*	.73*	.76*	.79*	.81*	.82*	.54*	.78*	.71*	.61*	.65*	.16	-.01	.19	.79*	.72*	.30*	.43*	1						
TCPP2	.22*	.06	.57*	-.01	.16	.59*	.35*	.53*	.73*	.62*	.65*	.56*	.54*	.45*	.26*	-.05	-.32*	-.26*	.54*	.46*	.02	-.06	.56*	1					
EHDPP	.32*	.39*	.02	.63*	.36*	-.01	.25*	.06	-.11	.12	-.13	.17	.06	.25*	.47*	.14	.44*	.48*	.16	.22*	.48*	.48*	.19	-.43*	1				
TBOEP	-.02	.29*	-.22*	.35*	.21*	-.30*	-.02	-.21	-.35*	-.20	-.36*	-.17	-.20	-.13	.08*	.05	.25*	.44*	-.20	-.14	.04	.20	-.08	-.69*	.66*	1			
TmCP	.56*	.55*	.58*	.50*	.59*	.52*	.64*	.57*	.50*	.59*	.46*	.60*	.48*	.47*	.62*	.29*	.22*	.32*	.59*	.56*	.59*	.5*2	.76*	.30*	.43*	-.02	1		
TpCP	.38*	.46*	.37*	.41*	.45*	.35*	.38*	.27*	.31*	.46*	.35*	.44*	.43*	.45*	.50*	.01	.01	.17	.44*	.42*	.25*	.15	.47*	.21	.35*	.04	.56*	1	
T2iPPP	.38*	.42*	.56*	.31*	.46*	.47*	.57*	.53*	.50*	.44*	.35*	.42*	.34*	.20	.28*	.29*	.21	.25*	.48*	.41*	.43*	.46*	.59*	.28*	.12	-.04	.58*	.26*	1

*p<0.05

Strength of the correlation
.00-.19 very weak
.20-.39 weak
.40-.59 moderate
.60-.79 strong
.80-1.0 very strong

Table S5.5. Air concentrations* of flame retardants (ng/m³) by task in e-recycling 2017-18.

	Supervision	Forklift operation	Manual handling	Bailer operation	Dismantling
BDE47					
GM [95% C.I.]	1 [.68-1.6]	1.6 [1.3-2.1]	2.4 [1.8-3]	2.1 [1.3-3.3]	2.2 [1.9-2.6]
GSD [95% C.I.]	1.8 [1.4-2.8]	1.8 [1.6-2.2]	1.8 [1.6-2.3]	1.6 [1.3-2.8]	2 [1.8-2.2]
AM [95% C.I.]	1.2 [.84-2.2]	2 [1.6-2.7]	2.9 [2.2-3.9]	2.4 [1.6-4.7]	2.8 [2.3-3.4]
BDE99					
GM	1.6 [.95-2.7]	2.8 [2.1-3.6]	4.4 [3.2-5.9]	3.6 [2.2-5.8]	3.7 [3.1-4.5]
GSD	2 [1.6-3.4]	1.9 [1.6-2.3]	2.1 [1.8-2.8]	1.6 [1.3-2.9]	2.1 [1.8-2.4]
AM	2 [1.3-4.6]	3.4 [2.6-4.7]	5.8 [4.3-8.9]	4.1 [2.7-8.3]	4.8 [4-6.1]
BDE209					
GM	290 [80-1100]	970 [460-2000]	1500 [770-3000]	3200 [1100-8900]	810 [520-1300]
GSD	6.1 [3.5-18]	6 [4.1-11]	5.1 [3.6-8.9]	3.2 [2.1-8.1]	6 [4.6-8.7]
AM	1500 [380-29000]	4900 [2000-22000]	5800 [2600-21000]	6200 [2400-43000]	4100 [2200-9800]
ATE					
GM	.33 [.24-.45]	.14 [.07-.28]	.12 [.052-.26]	.3 [.21-.42]	.079 [.045-.13]
GSD	1.5 [1.3-2.1]	4.9 [3.3-9.8]	6.3 [3.9-15]	1.4 [1.2-2.2]	6.6 [4.6-11]
AM	.36 [.28-.54]	.52 [.24-2.2]	.67 [.26-4.5]	.31 [.24-.51]	.48 [.24-1.5]
OBIND					
GM	5.8 [1.3-20]	13 [5.2-30]	17 [6.2-40]	59 [27-130]	11 [5.9-19]
GSD	5.5 [2.9-21]	7.5 [4.5-17]	8.8 [5.1-22]	2.3 [1.7-5.1]	9.1 [6.1-16]
AM	26 [7.1-590]	99 [33-850]	180 [51-2200]	86 [44-320]	130 [50-540]
PBT					
GM	.12 [.048-.29]	.1 [.046-.21]	.22 [.14-.34]	.24 [.16-.36]	.2 [.13-.3]
GSD	3.3 [2.1-8.2]	6 [3.7-13]	2.8 [2.2-4.1]	1.5 [1.2-2.6]	4.8 [3.7-7]
AM	.26 [.11-1.4]	.51 [.2-3]	.37 [.24-.71]	.26 [.19-.47]	.7 [.42-1.5]
aDP					
GM	2.2 [.76-6.5]	6.9 [4.6-10]	9.1 [5.4-15]	14 [5.5-34]	8.7 [6.4-12]
GSD	4.3 [2.7-11]	2.7 [2.1-3.8]	3.5 [2.6-5.4]	2.7 [1.8-6.3]	3.5 [2.9-4.6]
AM	6.4 [2.3-54]	11 [7.4-21]	20 [12-47]	23 [10-110]	19 [13-32]
sDP					
GM	1.2 [.43-3.5]	3.7 [2.6-5.4]	5.3 [3.3-8.6]	7.5 [3.2-17]	6.2 [4.6-8.1]
GSD	4.2 [2.7-10]	2.5 [2-3.4]	3.2 [2.5-4.8]	2.5 [1.7-5.6]	3.1 [2.6-3.8]
AM	3.5 [1.2-28]	5.7 [3.9-9.7]	11 [6.3-22]	12 [5.6-48]	12 [8.4-17]
TPhP					
GM	83 [46-150]	89 [61-130]	130 [93-190]	230 [150-360]	120 [99-150]
GSD	2.2 [1.7-3.8]	2.5 [2-3.5]	2.4 [2-3.3]	1.5 [1.3-2.7]	2.3 [2-2.7]
AM	110 [68-270]	140 [93-240]	200 [140-330]	250 [180-480]	170 [140-220]
TDCiPP					
GM	7.3 [4.3-12]	14 [11-17]	15 [11-20]	22 [14-33]	24 [19-30]
GSD	2 [1.6-3.4]	1.8 [1.5-2.2]	2 [1.7-2.7]	1.5 [1.2-2.6]	2.7 [2.3-3.3]
AM	9.4 [6-21]	16 [13-22]	19 [14-28]	24 [17-44]	39 [30-55]
TCEP					
GM	79 [49-130]	95 [81-110]	110 [92-130]	110 [67-190]	140 [120-150]
GSD	2 [1.5-3.3]	1.5 [1.3-1.7]	1.6 [1.4-1.8]	1.7 [1.3-3.1]	1.5 [1.4-1.6]
AM	100 [65-210]	100 [88-120]	120 [100-150]	130 [85-280]	150 [130-160]

95th perc., 95th percentile; AM: arithmetic mean; GM: geometric mean; GSD: geometric standard deviation

* Arithmetic and geometric means, as well as the geometric standard deviations, were calculated using a Bayesian model and a Markov chain simulation engine (see the methods section of the paper)

Table S5.6. Air conc.* of flame retardants (ng/m³) by material handled in e-recycling 2017-18.

	General	Miscellaneous electronics	Miscellaneous components	LCDs/LED/ Plasma screens	CRTs
BDE47					
GM [95% C.I.]	1.2 [.78-1.9]	1.6 [1.4-2]	1.9 [1.6-2.2]	2.8 [2-3.9]	2.8 [2.3-3.6]
GSD [95% C.I.]	2.3 [1.8-3.5]	1.7 [1.6-2]	1.5 [1.4-1.8]	2.1 [1.7-2.8]	1.8 [1.6-2.2]
AM [95% C.I.]	1.7 [1.1-3.4]	1.9 [1.6-2.4]	2.1 [1.8-2.5]	3.7 [2.6-5.8]	3.4 [2.7-4.5]
BDE99					
GM	2.1 [1.2-3.7]	2.7 [2.2-3.2]	3.1 [2.6-3.8]	4.7 [3.3-6.7]	5.3 [4.1-6.9]
GSD	2.8 [2.1-4.8]	1.8 [1.6-2.1]	1.6 [1.4-1.8]	2.2 [1.8-2.9]	1.9 [1.7-2.4]
AM	3.6 [2.1-9.2]	3.1 [2.6-3.9]	3.5 [2.9-4.3]	6.4 [4.5-10]	6.7 [5.2-9.3]
BDE209					
GM	200 [64-600]	570 [310-1000]	960 [570-1600]	1500 [710-3100]	3100 [2000-4900]
GSD	7.7 [4.5-19]	6.2 [4.4-9.9]	3.7 [2.8-5.7]	5 [3.4-9.3]	3.2 [2.5-4.7]
AM	1600 [410-21000]	3000 [1400-9600]	2300 [1300-5400]	5500 [2300-23000]	6200 [3800-13000]
ATE					
GM	.23 [.12-.42]	.09 [.048-.16]	.084 [.038-.17]	.13 [.048-.3]	.16 [.072-.31]
GSD	3 [2.2-5.4]	5.4 [3.6-10]	5.4 [3.4-12]	6.5 [3.8-16]	5.8 [3.7-12]
AM	.42 [.23-1.2]	.37 [.18-1.3]	.35 [.15-1.8]	.75 [.26-6.4]	.73 [.31-3.5]
OBIND					
GM	2.3 [.32-9.1]	2.8 [.76-7.5]	17 [8.3-32]	29 [15-53]	51 [34-76]
GSD	12 [5.2-64]	19 [9.1-63]	5.2 [3.5-10]	3.8 [2.7-6.7]	2.7 [2.2-3.9]
95th	130 [27-1900]	340 [98-2300]	250 [110-880]	260 [120-810]	270 [160-550]
AM	53 [8.1-8000]	210 [35-10000]	65 [29-270]	71 [36-220]	86 [57-150]
PBT					
GM	.04 [.0093-.12]	.13 [.078-.2]	.16 [.098-.25]	.24 [.14-.4]	.51 [.34-.76]
GSD	8.1 [4.1-31]	4.1 [3-6.4]	3.2 [2.4-5.1]	3.1 [2.4-5.1]	2.9 [2.3-4]
AM	.36 [.088-12]	.34 [.2-.78]	.32 [.19-.69]	.46 [.27-1.1]	.88 [.57-1.6]
aDP					
GM	2 [.92-4.5]	5.5 [4.1-7.5]	7.1 [4.9-10]	14 [8.3-25]	19 [13-28]
GSD	4.2 [2.9-8.2]	2.6 [2.1-3.3]	2.5 [2-3.4]	3.3 [2.5-5.3]	2.9 [2.3-4.1]
AM	5.9 [2.5-25]	8.6 [6.2-13]	11 [7.4-18]	29 [16-71]	33 [21-61]
sDP					
GM	1.1 [.52-2.4]	3.8 [3-4.8]	4.2 [3.1-5.8]	7.9 [4.7-14]	12 [8.7-17]
GSD	4.1 [2.8-8]	2.1 [1.8-2.6]	2.2 [1.8-2.9]	3.3 [2.4-5.2]	2.4 [2-3.3]
AM	3.1 [1.4-13]	5 [3.9-6.9]	5.8 [4.2-8.8]	16 [9.2-40]	18 [13-30]
TPhP					
GM	67 [38-120]	98 [77-120]	98 [71-140]	170 [120-260]	180 [140-230]
GSD	2.8 [2.1-4.6]	2 [1.8-2.5]	2.3 [1.9-3.1]	2.4 [2-3.5]	1.9 [1.6-2.4]
AM	110 [66-280]	130 [100-170]	140 [100-220]	260 [170-470]	220 [170-300]
TDCiPP					
GM	6.7 [4.4-10]	16 [12-23]	16 [13-20]	25 [17-37]	29 [22-38]
GSD	2.2 [1.7-3.2]	2.8 [2.3-3.6]	1.7 [1.5-2]	2.3 [1.9-3.3]	1.9 [1.7-2.4]
AM	9.1 [6.1-17]	28 [19-44]	19 [15-24]	36 [24-63]	36 [28-50]
TCEP					
GM	87 [63-120]	110 [95-120]	100 [88-120]	140 [120-160]	160 [130-190]
GSD	1.8 [1.5-2.5]	1.4 [1.3-1.5]	1.5 [1.4-1.7]	1.4 [1.3-1.6]	1.6 [1.4-1.9]
AM	100 [77-160]	110 [100-130]	110 [96-140]	140 [120-170]	170 [150-210]

95th perc., 95th percentile; AM, arithmetic mean; GM geometric mean; GSD, geometric standard deviation
* Arithmetic and geometric means, as well as the geometric standard deviations, were calculated using a Bayesian model and a Markov chain simulation engine (see the methods section of the paper)

Table S5.7. Exponentiated Tobit regression coefficients for each flame retardant in e-recycling facilities. 2017-2018.

	n	PBDEs			NBFRs			ClFRs		OPEs		
		BDE47	**BDE99**	**BDE209**	**ATE**	**OBIND**	**PBT**	**aDP**	**sDP**	**TDCiPP**	**TPhP**	**TCEP**
Task[a]												
Supervision	6	1.0 (Comparison category)										
Forklift operating	17	1.9 [1.1–3.1]	2.1 [1.2–3.7]	3.3 [1.5–7.4]	.67 [.18–2.5]	2.4 [.64–8.9]	1.0 [.34–2.7]	3.0 [1.5–5.8]	3.0 [1.5–5.9]	1.8 [.93–3.6]	1.1 [.66–1.8]	1.2 [.81–1.6]
Manual handling	17	1.9 [1.1–3.1]	2.2 [1.3–3.7]	2.7 [1.2–6.0]	.24 [.065–.87]	2.0 [.55–7.6]	1.1 [.41–3.1]	2.8 [1.4–5.4]	3.1 [1.6–6.0]	1.7 [.89–3.4]	1.2 [.73–2.0]	1.4 [.96–1.9]
Bailer operating	4	2.0 [.99–3.9]	2.1 [1.0–4.]	3.5 [1.2–10]	.86 [.15–4.8]	3.3 [.62–18]	1.0 [.26–4.0]	2.9 [1.2–7.2]	3.3 [1.3–8.2]	2.2 [.90–5.4]	1.8 [.90–3.5]	1.4 [.84–2.2]
Dismantling	44	2.0 [1.2–3.1]	2.2 [1.4–3.7]	3.6 [1.7–7.6]	.41 [.13–1.4]	2.9 [.84–9.9]	1.5 [.57–3.9]	4.6 [2.5–8.5]	5.8 [3.1–1.8]	2.7 [1.4–4.9]	1.6 [.97–2.5]	1.6 [1.2–2.3]
Sex												
Woman	20	1.2 [.91–1.7]	1.4 [.98–1.9]	.83 [.51–1.4]	1.3 [.59–3.0]	.68 [.32–1.4]	1.1 [.61–2.1]	.77 [.51–1.2]	.77 [.51–1.2]	.90 [.60–1.4]	.90 [.66–1.2]	.93 [.75–1.2]
Duration of employment (3 years increments)		.85 [.76–.94]	.83 [.74–.93]	.80 [.68–.94]	.75 [.56 – 1.0]	.86 [.65–1.1]	.73 [.58–.92]	.89 [.77–1.0]	.88 [.76–1.0]	.87 [.76–1.0]	.87 [.79–.97]	1.0 [.93–1.1]
Facility size												
Small	22	1.0 (Comparison category)										
Medium	30	1.1 [.80–1.6]	1.1 [.75–1.5]	4.4 [2.6–7.3]	.26 [.11–.63]	11 [4.7–26]	4.6 [2.4–9.0]	2.5 [1.3–3.9]	2.1 [1.4–3.2]	2.3 [1.5–3.5]	1.8 [1.3–2.5]	1.2 [.96–1.5]
Large	36	1.3 [.96–1.8]	1.6 [1.1–2.2]	38 [23–62]	2.2 [.97–4.9]	59 [25–136]	8.3 [4.4–16]	9.4 [6.2–14]	6.4 [4.3–9.7]	2.0 [1.3–3.0]	3.9 [2.9–5.3]	1.0 [.80–1.2]
Material treated[b]												
General/None	10	1.0 (Comparison category)										
Miscellaneous electronics	27	1.3 [.90–2.0]	1.3 [.83–2.0]	3.1 [1.8–5.4]	.44 [.16–1.2]	1.7 [.68–4.1]	2.5 [1.2–5.5]	2.8 [1.8–4.5]	3.5 [2.2–5.7]	2.5 [1.5–4.1]	1.5 [1.0–2.2]	1.2 [0.9–1.6]
LCDs/LED/Plasma screens	14	2.2 [1.4–3.5]	2.2 [1.3–3.7]	5.4 [2.9–10]	1.0 [.33–3.3]	5.4 [2.0–14]	2.8 [1.1–6.7]	6.0 [3.5–10]	6.4 [3.7–11]	2.8 [1.6–5.1]	2.3 [1.4–3.5]	1.5 [1.1–2.1]
Miscellaneous components	18	1.5 [1.0–2.3]	1.5 [.93–2.4]	4.3 [2.4–7.7]	.49 [.17–1.4]	4.5 [1.8–12]	2.5 [1.1–5.7]	3.3 [2.0–5.5]	3.6 [2.2–6.1]	2.2 [1.3–3.8]	1.4 [0.9–2.1]	1.2 [.89–1.6]
Cathode ray tubes	19	2.2 [1.4–3.4]	2.4 [1.5–3.8]	7.7 [4.2–14]	.84 [.28–2.5]	6.9 [2.8–18]	5.4 [2.3–12]	6.3 [3.7–10]	8.2 [4.9–14]	3.3 [1.9–5.8]	2.0 [1.3–3.0]	1.8 [1.4–2.4]

	n	PBDEs			NBFRs			ClFRs		OPEs		
		BDE47	**BDE99**	**BDE209**	**ATE**	**OBIND**	**PBT**	**aDP**	**sDP**	**TDCiPP**	**TPhP**	**TCEP**
Facility size												
Small	22	1.0 (Comparison category)										
Medium	30	1.1	1.1	3.7	.28	6.6	4.6	1.9	1.6	2.2	1.7	1.0
		[.8–1.6]	[.77–1.6]	[2.3–5.7]	[.12–.67]	[3.2–14]	[2.5–8.7]	[1.3–2.8]	[1.1–2.4]	[1.5–3.4]	[1.2–2.3]	[.84–1.3]
Large	36	1.3	1.5	34	2.5	42	7.6	7.2	4.7	1.9	3.8	.86
		[1.0–1.8]	[1.1–2.1]	[22–51]	[1.2–5.4]	[21–85]	[4.2–14]	[5.0–10]	[3.3–6.8]	[1.3–2.8]	[2.8–5.1]	[.71–1.1]

LCDs, liquid crystal displays; LEDs, light-emitting diode displays.

[a] Model A, tasks adjusted for sex, duration of employment (3-year increments) and facility size

[b] Model B, material treated adjusted for facility size.

Table S5.8. Cox hazard ratios for each flame retardant in e-recycling facilities. 2017-2018.

	n	BDE47	BDE99	BDE209	ATE	OBIND	PBT	aDP	sDP	TDCiPP	TPhP	TCEP
Task[a]												
Supervision	6	1 (Comparison category)										
Forklift operating	17	2.9*	3.3*	3.2*	0.70	3.6*	1.6	4.9*	4.4*	1.9	2.1	1.9
Manual handling	17	2.7	2.6	3.5*	0.33*	4.7*	1.4	6.4*	6.6*	2.4	2.6	3.0*
Bailer operating	4	4.7*	5.0*	6.7*	1.1	9.1*	1.7	8.9*	9.6*	4.3*	7.7*	3.8
Dismantling	44	3.5*	5.1*	6.9*	0.56	8.0*	3.4*	17*	24*	5.0*	6.3*	6.2*
Woman	20	1.8	1.65	0.80	1.4	0.55	1.1	0.67	0.65	0.66	0.97	1.0
Years of employment (3)		0.72*	0.76*	0.83	0.92	1.0	0.98	0.93	0.87	0.96	0.78*	1.1
Facility size												
Small	22	1 (Comparison category)										
Medium	30	1.9	2.2*	7.0*	0.54	3.7*	4.0*	4.9*	4.6*	14*	3.8*	2.6*
Large	36	2.1*	4.0*	420*	2.4*	54*	11*	145*	66*	8.8*	33*	1.4
Material treated[b]												
General/none	10	1 (Comparison category)										
Misc electronics	27	1.8	2.3*	3.4*	0.52	2.3*	2.2*	6.0*	6.4*	3.0*	2.6*	2.8*
LCDs/LED/Plasma screens	14	3.6*	5.4*	10*	0.97	6.9*	2.7*	21*	15*	4.9*	8.7*	4.1*
Misc components	18	2.3	2.9*	5.1*	0.48	3.8*	1.9	7.1*	7.2*	3.3*	2.9*	2.2
CRTs	19	3.8*	6.4*	20*	0.98	14*	7.5*	24*	32*	6.6*	6.9*	6.4*
Facility size												
Small	22	1 (Comparison category)										
Medium	30	2.1*	2.1*	5.9*	0.49*	2.1*	3.7*	2.6*	2.1*	8.3*	3.8*	2.0*
Large	36	2.4*	3.4*	593*	2.2	40*	7.6*	83*	24*	5.3*	28*	0.92

* P<0.05

[a] Model A, tasks adjusted for sex, duration of employment (3-year increments) and facility size

[b] Model B, material treated adjusted for facility size.

5.8.2. Supplementary material references

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Chapitre 6. Multi-exposures to suspected endocrine disruptors in electronic waste recycling workers: associations with thyroid and reproductive hormones.

Multi-exposures to suspected endocrine disruptors in electronic waste recycling workers: associations with thyroid and reproductive hormones.

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Cet article répond au dernier objectif de cette thèse, soit celui d'explorer les effets endocriniens associés à l'exposition aux ignifuges, et d'explorer les effets d'expositions multiples.

Les analyses statistiques et la rédaction du manuscrit ont été effectuées par l'étudiante. Le manuscrit a été révisé et approuvé par tous les coauteurs.

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6.1. Abstract

Electronic waste recycling (e-recycling) exposes workers to substances such as flame retardants and metals. Some of them are known or suspected endocrine disruptors that could affect hormonal homeostasis and eventually result in adverse health outcomes. Our aim was to measure biological concentrations of organophosphate ester (OPE) metabolites, polybrominated diphenyl ethers (PBDEs), mercury, lead and cadmium in e-recycling workers, and to explore associations with thyroid and sexual hormones.

In a cross-sectional study, end-of-shift blood and urine spot samples were collected from 23 women and 77 men in six e-recycling facilities and one commercial recycling facility. Urinary concentrations of 15 OPE metabolites and mercury, and blood concentrations of 12 PBDE congeners, lead, cadmium, and thyroid (thyroxine [T4], triiodothyronine [T3], thyroid stimulating hormone [TSH]) and sexual (testosterone [T], estradiol, Follicle Stimulating Hormone [FSH], Luteinizing hormone [LH]) hormones were measured.

E-recycling workers had higher concentrations of BDE209, all OPE metabolites, and lead than commercial recycling workers. In e-recycling workers, plasma geometric mean concentration of BDE209 was 18 ng/g lipids (geometric standard deviation [GSD]: 2.8) vs.1.7 ng/g lipids (GSD: 2.8) in commercial recycling, and urinary geometric mean concentration of diphenyl phosphate (DPhP), a major metabolite of triphenyl phosphate, was 1.7 ng/ml (GSD: 2.5), vs. 0.95 ng/ml (GSD: 2.0). In men, a two-fold increase in BDE209 was associated with 3.1% (95% Confidence interval: 0.07, 6.1) higher levels of total T4, and a two-fold increase in tert-butyl diphenyl phosphate (tb-DPhP) was associated with 18% (-29, -4.7) lower total T, 18% (-27, -6.9) lower free T and 13% (-25, 0.70) lower free T/estradiol ratio. In women, a two-fold increase in BDE153 was associated with 10% (-17, -3.2) lower free T3.

To our knowledge, this is the first study to show associations between OPE metabolites and sex hormones in adults. Although some of our results are not conclusive and need replication, they suggest that prudent avoidance should be applied in risk management of flame retardants.

6.2. Introduction

Flame retardants (FRs) are added to common goods such as electronics, fabric, plastic and foam in order to meet fire safety regulations. Most of these chemicals are semi-volatile and are not bound to the materials to which they are added. They can be released in the air or adsorb to dust and particulate matter that is in contact with the materials (Kemmlein et al. 2003; Takigami et al. 2008). For many years, the most commonly used FRs in the North American electronic equipment manufacturing have been polybrominated diphenyl ethers (PBDEs) (Abbasi et al. 2016; La Guardia et al. 2006), but their bioaccumulative and toxic properties justified a ban in their production and use in several countries over the past decades (Abbasi et al. 2015). PBDEs were therefore gradually replaced by less persistent substances such as novel brominated FRs and organophosphate esters (OPEs) (Covaci et al. 2011).

Owing to FRs' continuous prevalence in the environment, biological background levels have been measured in the general population (Butt et al. 2014; Gravel et al. 2018). Indeed, employed adults from national health surveys had a median 2,2',4,4'-tetrabromodiphenyl ether (BDE47) blood level of 19 ng/g lipids in the United States in 2003-2004, and 10 ng/g lipids in Canada in 2007-2009 (Gravel et al. 2018). The gradual shift in FR chemical group usage was paralleled around the 2000s by a decline in the general population's biological PBDEs levels in America (Cowell et al. 2019), although they appear to have plateaued and increased again more recently (Hurley et al. 2017; Parry et al. 2018). OPE exposure biomarker levels appear to be on the rise (Hoffman et al. 2017a), with the most recent median urinary concentration of diphenyl phosphate (DPhP) (a metabolite of triphenyl phosphate [TPhP] and ethylhexyldiphenyl phosphate [EHDPP], among others) in US adults measured at 0.76 ng/ml (Ospina et al. 2018). Exposure routes are thought to be through ingestion of certain foods (e.g., meat, fish) and dust, and through dermal contact, as well as inhalation (Abou-Elwafa Abdallah et al. 2016; Bramwell et al. 2017). Careful interpretation of the biomarkers is warranted as FR human biological half-lives are not well documented (Gravel et al. 2019a). In addition, biological levels can be influenced by age, sex, body mass index and ethnicity among other factors (Ospina et al. 2018). Some occupations have been shown to expose workers to high concentrations of PBDEs and OPEs (Gravel et al. 2019a). Among occupations with the highest recorded median biological levels of FRs, we find firefighting (BDE47: 30 ng/g lipid in plasma) (Park et al. 2015), foam recycling (BDE47: 78 ng/g lipid in plasma) (Stapleton et al. 2008), and flight crews (DPhP: 302 ng/ml in urine) (Schindler et al. 2013).

There is increasing evidence that many FRs can have adverse effects, and notably that they can act as endocrine disruptors for thyroid and reproductive hormones (Dishaw et al. 2014; Gore 2007). Endocrine disrupting chemicals can interfere with any aspect of hormone action, sometimes at the subclinical level (Gore et al. 2015). Endocrine effects have been quantified and documented fairly consistently *in vitro* (Hill et al. 2018; Li et al. 2010), *in vivo* (Lilienthal et al. 2006; Pinson et al. 2016), and in newborns and children (Jacobson et al. 2016; Vuong et al. 2018). However, the few studies in adults report discordant effects of FRs on thyroid and reproductive hormones (Supplementary Table 1). For instance, some epidemiological studies in low to moderately-exposed populations (median serum BDE47 from 0.21 to 7.9 ng/g lipids) have reported that BDE47 exposure was associated with lower levels of total thyroxine (totalT4) (Abdelouahab et al. 2011; Makey et al. 2016a) and total triiodothyronine (totalT3) (Huang et al. 2014; Kim et al. 2013), while others did not detect any association (Bloom et al. 2008; Byrne et al. 2018; Eguchi et al. 2015). On the other hand, BDE47 was associated with higher levels of totalT3 or totalT4 in more highly exposed populations (geometric mean serum BDE47 from 17 to 78 ng/g lipids) (Stapleton et al. 2011; Zheng et al. 2017). There is still a need for research on the endocrine effects of FRs in moderately to highly-exposed adult sub-populations that can complement research conducted on the general population. Additionally, the concurrent exposure to many FRs and to other potential endocrine disruptors such as lead, cadmium or mercury (Chen et al. 2013) may have endocrine effects that are insufficiently documented thus far (Crofton 2008; Curcic et al. 2014). Because hormonal levels are influenced by numerous factors that are difficult to control in field studies, it has been recommended to also look at ratios of hormone concentrations, which can provide insights into the capacity of the endocrine system to co-regulate and respond to homeostasis disruptions (Koulouri et al. 2013; Sollberger and Ehlert 2016),

The North American electronic manufacturing industry has used FRs in large quantities in the past five decades (up to an estimated 35,000 tons of decaBDE in cathode ray tube TVs in 2000) (Abbasi et al. 2015). Thus the electronic waste recycling (e-recycling) industry can be expected to harbor some of the highest occupational concentrations, but little is known on the levels of FRs or on the occupational health and safety practices in that industry (Bakhiyi et al. 2018). In 2017-2018, we conducted a cross-sectional study aiming to describe the occupational health and safety practices, total airborne particulate matter (PM), and metal and flame retardant exposures in a few Canadian e-recycling facilities. We assessed exposure through air sampling (Gravel et al. 2019b) and biomarkers, and measured hormone levels. The aim of this article is to report biological concentrations of plasma PBDEs and urinary OPEs metabolites, as well as mercury, cadmium and lead, and to explore their associations with concentrations of thyroid and reproductive hormones in e-recycling and commercial recycling workers.

6.3. Materials and methods

6.3.1. Study design and participants

Six e-recycling companies, and one non-e-recycling company participated in our study. The latter served as a comparison group with low-exposure to FRs and consisted of a commercial waste recycling company (mainly glass, and a small proportion of cardboard and metal). Eligible participants had to be working in the facility for at least one month, to be over 18 years old and to be directly or indirectly in contact with electronic or commercial waste. Sampling took place between May 2017 and March 2018. Characteristics of the facilities and the detailed study design are presented in Gravel et al. (2019b). Briefly, the 100 participating workers who completed the study provided urine samples at the end of their work shift on a Wednesday, and blood samples at the end of their shift on the following day. They were also individually interviewed to collect sociodemographic data (age, duration of employment in the facility, country of birth), medical information (endocrine diseases and medication intake), various personal habits (smoking status, hand washing), and use of personal protective equipment. The body mass index (BMI) was calculated from the height and weight of the participants, which were measured by a research team member.

The study protocol and documents were reviewed and approved by the Université de Montréal Human Health Research Ethics board. All participants signed an informed consent form and received a financial compensation. An occupational physician from the research team (Dr. Patry) reviewed hormonal values and metals concentration above the obligatory reporting values, to ensure a follow-up for workers if need be.

6.3.2. Specimen collection and analyses

PBDEs were analyzed in serum samples and OPE metabolites were analyzed in urine samples. Table 1 lists the names of all biomarkers. Lead (Pb) and cadmium (Cd) were analyzed in blood, and mercury (Hg) in urine for comparison with occupational biological exposure indices (BEI®) (American Conference of Governmental Industrial Hygienists 2019). The details of specimen collection, transportation, storage and analysis are found in the Supplementary material.

A registered nurse proceeded to the blood draw after the work shift. Blood samples for Cd, Pb and PBDEs were kept at room temperature and centrifuged or stored at 4°C on the same day, and the blood samples for hormone analyses were centrifuged onsite before being taken to the laboratory for analysis. Blood Cd was analysed at the Centre de toxicologie du Québec (CTQ; Institut national de santé publique du Québec, Québec City, Canada) by inductively coupled plasma mass spectrometry and blood Pb was analysed at the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) laboratory by graphite furnace atomic absorption spectrometry. The PBDE congeners listed in Table 1 were analysed in serum samples by gas chromatography-mass spectrometry. Blood lipids (sum of triglycerides and total cholesterol) were analysed at the CTQ. Hormone analyses (total and free T3 and T4, thyroid stimulating hormone [TSH], total and free testosterone, follicle stimulating hormone [FSH], luteinizing hormone [LH] and estradiol [E2]) were performed by a privately-owned clinical laboratory following standard clinical procedures by chemiluminescent immunoassays, except for totalT in women which was analysed by liquid chromatography-mass spectrometry.

End-of shift urine samples were collected in polyethylene bottles and transported on ice to the IRSST. They were frozen at -70°C for OPE analyses and kept at 4°C for Hg analysis. Urinary Hg concentrations were determined at the IRSST by cold vapor atomic absorption spectrometry. Urinary OPE metabolites listed in Table 1 were analysed at the CTQ by ultra performance liquid chromatography with a tandem mass spectrometer. Urine specific gravity and creatinine were analyzed in the respective laboratories for each analysis.

Table 6.1. Biological indicators of exposure to polybrominated diphenyl ethers, organophosphate esters and metals in serum and urine, with their limit of detection and percentage of detection, in e-recycling and other commercial recycling workers.

Biological indicator	Abbrev.	LOD (ng/ml)	% > LOD Commercial	% > LOD E-waste	
PBDEs (Parent compound in serum)					
4,4'-Dibromodiphenyl ether	BDE15	0.03	0	0	
2,2',4-Tribromodiphenyl ether	BDE17	0.03	0	0	
2,3',4-Tribromodiphenyl ether	BDE25	0.03	0	0	
2,4,4'-Tribromodiphenyl ether	BDE28	0.03	0	2	
2',3,4-Tribromodiphenyl ether	BDE33	0.03	0	0	
2,2',4,4'-Tetrabromodiphenyl ether	BDE47	0.03	67	42	
2,2',4,4',5-Pentabromodiphenyl ether	BDE99	0.02	20	18	
2,2',4,4',6-Pentabromodiphenyl ether	BDE100	0.02	20	18	
2,2',4,4',5,5'-Hexabromodiphenyl ether	BDE153	0.03	67	44	
2,2',4,4',5,6'-Hexabromodiphenyl ether	BDE154	0.01	7	5	
2,2',3,4,4',5',6-Heptabromodiphenyl ether	BDE183	0.01	0	24	
Decabromodiphenyl ether	BDE209	0.02	27	89	
OPEs (Metabolites in urine)					**Known parent compound**
Bis (2-butoxyethyl) phosphate	BBOEP	0.1	13	31	Tris(2-butoxyethyl) phosphate (TBOEP)
Bis (2-chloroethyl) carboxymethyl phosphate	BCECMP	0.1	47	69	Tris(2-chloroethyl) phosphate (TCEP)
Bis (2-chloroethyl) 2-hydroxyethyl phosphate	BCEHEP	0.05	27	48	Tris(2-chloroethyl) phosphate (TCEP)
Bis (2-chloroisopropyl) carboxyethyl phosphate	BCiPCEP	0.2	53	76	Tris(1-chloro-2-propyl) phosphate (TCiPP)
Bis (1-chloro-2-propyl) 1-hydroxy-2-propyl phosphate	BCiPHiPP	0.2	87	98	Tris(1-chloro-2-propyl) phosphate (TCiPP)
Bis (1,3-dichloropropyl) phosphate	BDCiPP	0.5	47	50	Tris(1,3-dichloro-2-propyl) phosphate (TDCiPP)
Dibutyl phosphate	DBP	0.4	7	22	Tris-n-butyl phosphate (TnBP)
Diisobutyl phosphate	DiBP	0.02	67	26	Triisobutylphosphate (TiBP)
Diisopropyl phosphate	DiPP	0.04	7	5	Triisopropylphosphate (TiPP)

Biological indicator	Abbrev.	LOD (ng/ml)	% > LOD Commercial	E-waste	
Diphenyl phosphate	DPhP	0.2	100	97	Triphenyl phosphate (TPhP) 2-Tert-butylphenyl diphenyl phosphate (BPDP) Resorcinol bis(diphenyl phosphate) (PBDPP) Ethylhexyldiphenyl phosphate (EHDPP) Isopropyl triphenyl phosphate (iP-TPhP)
Para-hydroxyphenyl phenyl phosphate	pOH-DPhP	0.04	47	74	Triphenyl phosphate (TPhP)
(4-hydroxyphenyl) diphenyl phosphate	pOH-TPhP	0.02	40	38	Triphenyl phosphate (TPhP)
Ortho-isopropylphenyl phenyl phosphate	o-iPr-DPhP	0.02	40	56	Ortho-isopropylphenyl diphenyl phosphate (iP-TPhP)
Para-isopropylphenyl phenyl phosphate	p-iPr-DPhP	0.02	13	17	Para-isopropylphenyl diphenyl phosphate (iP-TPhP)
Tert-butyl diphenyl phosphate	tb-DPhP	0.02	33	60	Tert-butyl triphenyl phosphate (tb-TPhP)
Metals					
Cadmium (blood)	Cd	0.04	100	95	
Lead (blood)	Pb	1.9	27	46	
Mercury (urine)	Hg	0.03	0	32	

LOD, limit of detection; ng/ml, nanograms per milliliter of elutriate

6.3.3. Statistical analysis

Data preparation

PBDE serum concentrations were presented on a total lipid-adjusted basis, calculated as 1.677*(total cholesterol – free cholesterol) + free cholesterol + triglycerides + phospholipids (Patterson et al. 1991). OPE urinary concentrations were standardized on urine specific gravity as follows: Standardized concentration = [concentration of metabolite * (1.024 - 1)] / [specific gravity - 1] (Gagné 2019). Urinary mercury was adjusted on creatinine concentration by dividing the concentration of Hg in urine by the creatinine concentration (Gagné et al. 2018a). The following ratios were calculated: free/totalT3, free/totalT4, freeT4/freeT3, free/totalT and freeT/E2. Visual inspection of data histograms suggested the lognormal distribution as a better model than the Gaussian distribution for all metrics, which was confirmed by Q-Q plots. Hence, contaminants, hormones and hormone ratios were natural log transformed. For Spearman's correlations, values below the LOD were substituted with the limit of detection divided by the square root of two. For linear regressions and principal component analyses, biomarkers' values below the limit of detection were also substituted with the limit of detection divided by the square root of two, which still provided some variability as the concentrations were standardized for lipids, specific gravity or creatinine levels (Farnham et al. 2002; Nie et al. 2010).

Exposure biomarker concentrations

Descriptive statistics were stratified on the type of facility (e-recycling and commercial recycling). We employed a bayesian model fit using a Monte Carlo Markov Chain (MCMC) engine assuming a log-normal distribution (www.expostats.ca toolkit, Lavoue et al. (2019)) to calculate the arithmetic and geometric means, and the arithmetic and geometric standard deviations, for FR biomarkers that were detected in at least 40% of samples and for estradiol (the only hormone with values below the limit of detection). This approach allows for an optimal treatment of left-censored data (values below the limit of detection) in univariate analyses (Huynh et al. 2016). Spearman's rank coefficients were calculated to assess correlations between PBDEs, OPEs and metals that were detected in at least 20% of samples, a percentage that allows consideration of most of the analytes (4 PBDE, 13 OPE and 3 metals in e-recycling; 5 PBDE, 11 OPE and 2 metals in commercial recycling). In order to identify multiple exposure profiles and reduce the dimensionality of our data while including all flame retardants regardless of collinearity, we carried out principle component analyses (PCA). PCA creates variables (components) that account for the maximum variance in the data, without being correlated with each other, which facilitates the identification of exposure patterns (Lever et al. 2017). Principal component analyses were done on biomarkers detected in at least 40% of samples in each group. The Kaiser-Meyer-Olkin (KMO) measure of sample adequacy was calculated and yielded an overall value of 0.46 for the e-recycling group, and 0.48 for the commercial recycling group, reflecting the presence of positive and negative correlations in the data (Cerny and Kaiser 1977; Kaiser 1974).

Association between flame retardants and hormone levels

Subjects with thyroid, pituitary gland or gonad diseases were excluded from the analyses involving the relevant hormones. Multiple linear regressions were used to assess associations between flame retardant biomarkers and hormone levels. For each hormone and ratio, the model included all biomarker concentrations that had an overall detection percentage above 40%, as well as covariables age (continuous), BMI (kilograms per meter squared, continuous), and current smoking (dichotomous). These covariables have been previously associated with biological levels of some flame retardants and can also influence certain hormone levels (Field et al. 1994; Fontes et al. 2013; Jain 2013). The analyses included participants from both types of facilities, and were stratified on sex. Because of high collinearity between some variables (spearman coefficient > 0.7), those with the lowest detection percentages were removed from the model. Hence, the biomarkers included were BDE47, BDE153, BDE209, BDCiPP, o-iPr-DPhP, tb-DPhP, BCECMP, DPhP, BCiPHiPP, Cd and Pb, after removal of BCiPCEP, pOH-DPhP and BCEHEP. Analyses on FSH, LH and E2 were only performed on men because we did not have data on women's menstrual cycle.

All hormones were above the limit of detection (LOD) in both men and women, except estradiol in men for which 24% of values were below the LOD of 60 pmol/l. To perform a regression with such a left-censored dependent variable, Tobit regression was employed, using the same covariables as in the linear regressions used for the other hormones; a Cox-Snell pseudo-R^2 was calculated for this analysis, a likelihood ratio test which reflects the improvement of the full model over the intercept-only model (transformation of likelihood ratio) (Deroche 2015).

We ran several sensitivity analyses. First, we excluded outliers that had an absolute value of studentized residuals greater than 3. We also excluded participants that had hormone values outside of the normal laboratory range (10 men and 1 woman for thyroid hormones; 63 men and 13 women for sex hormones). The final results presented include outliers and participants with hormone values outside of normal laboratory range. However the results exclude participants who had diseases of the thyroid or the pituitary gland in the analyses with thyroid hormones (3 men, 4 women), and participants with testes or pituitary disease in the sex hormones analyses (2 men). To ensure that there was no multicollinearity in the linear regressions, variance inflation factors (VIF) were calculated. They were all below 5, except for the analyses on women where 3 exposures variables had a VIF around 10, indicating an overall low collinearity in our models.

Statistical analyses were carried out using STATA version 15.1 (StataCorp LLC, Texas) and the statistical significance level was set at $\alpha = 0.05$.

6.4. Results

6.4.1. Workers characteristics

A total of 77 men and 23 women participated in the study (Table 2). Out of the 28 workers born outside Canada, 19 were from Central and South America, 4 from the Middle East, 4 from the African continent and one from North America. Three men and four women reported diseases affecting the thyroid, one man had a disease affecting the pituitary gland, and one man had a disease affecting the gonads. Duration of employment ranged from 1 month to 22 years, with a mean of 3.6 years.

Table 6.2. Characteristics of the study participants

Variable	**Categories**	**Commercial recycling n (%)**	**E-waste recycling n (%)**
Sex	Female	4 (27)	19 (22)
	Male	11 (73)	66 (78)
Age (years)	19–39	6 (40)	41 (48)
	40–59	7 (47)	43 (51)
	≥ 60	2 (13)	1 (1)
Country of birth	Other	0	28 (33)
	Canada	15 (100)	57 (67)
Body mass index (BMI, kg/m^2)	< 25	10 (67)	34 (40)
	25–29.9	1 (6)	20 (24)
	≥ 30	4 (27)	31 (36)
Education	< High school graduate	9 (60)	40 (47)
	High school graduate or equivalent	6 (40)	45 (53)
Smoking status	Past or non-smoker	7 (47)	57 (67)
	Current smoker	8 (53)	28 (33)
Duration of employment (months)	0-6	2 (13)	22 (26)
	7-36	7 (47)	25 (30)
	>=37	6 (40)	37 (44)
Frequency of hand washing per day (self-reported)	<2	1 (7)	0
	2-3	5 (33)	14 (17)
	4-5	1 (7)	30 (35)
	>5	8 (53)	41 (48)
Wearing nitrile gloves (observed)	No	15 (100)	62 (73)
	Yes	0	21 (25)
	Not applicable	0	2 (2)
Type of respiratory protection (observed)	N95	0	11 (13)
	N95 + mercury cartridges	0	8 (9)
	None	15 (100)	66 (78)

6.4.2. Biomarker concentrations

The percentages of values above the limit of detection for all biological indicators are presented in Table 1 and stratified on the type of industry (commercial recycling or e-recycling). Table 3 presents the arithmetic and geometric means, as well as the range for analytes that were detected in at least 40% of all samples, stratified by the type of industry. The highest geometric mean of PBDE congeners was observed for BDE209 in the serum of e-recycling workers (18 ng/g lipids, geometric standard deviation [GSD]: 2.8), and the highest geometric mean OPE metabolites were DPhP and BClPHiPP, both with 1.7 ng/ml in e-recycling workers (GSD: 2.5 and 3.0, respectively). Men generally had higher concentrations of FR biomarkers than women (2 to 69% higher), except for o-iPr-DPhP and pOH-DPhP (5 and 11% lower, respectively) (data not tabulated).

Correlations between the biomarkers for participants in e-recycling and in the comparison group are presented in Supplementary Table 2 and 3. In e-recycling, there was a strong correlation between blood lead and BDE209 levels (Spearman's ρ=0.63). There was a strong very strong correlation between BCiPCEP and BCiPHiPP (ρ=0.94), two known metabolites of tris(1-chloro-2-propyl) phosphate (TCiPP), as well as between two metabolites of tris(2-chloroethyl) phosphate (TCEP), namely BCECMP and BCEHEP (ρ=0.78). DPhP, which is a non-specific metabolite for many OPEs, was strongly correlated with BCECMP and pOH-DPhP (ρ=0.64 and 0.76), and pOH-DPhP was also strongly correlated with pOH-TPhP (ρ=0.75). In commercial recycling, there were moderate to very strong correlations between most OPE metabolites and strong to very strong correlations between BDE100 and BDE47 (ρ=0.64), and with BDE99 (ρ=0.98).

Table 6.3. Arithmetic mean, standard deviation, geometric mean, geometric standard deviation and range for hormones and for PBDEs and OPE exposure biomarkers that were detected in at least 40% of samples, in e-recycling and in commercial recycling workers[a].

		Commercial recycling (n=15)			**E-recycling** (n=85[b])			
		AM (SD)	**GM (GSD)**	**Range**	**AM (SD)**	**GM (GSD)**	**Range**	
Hormones								**Lab normal values**
freeT3 (pmol/L)		5.2 (0.55)	5.1 (1.1)	3.9–5.9	5.0 (0.55)	5.0 (1.1)	4.0–6.9	3.5–6.5
totalT3 (nmol/L)		1.5 (0.22)	1.5 (1.2)	1.1–1.9	1.6 (0.27)	1.6 (1.2)	0.88–2.3	0.92–2.8
freeT4 (pmol/L)		15 (2.7)	15 (1.2)	11–20	15 (1.9)	15 (1.1)	11–21	9.5–24
totalT4 (nmol/L)		87 (13)	86 (1.2)	70–114	89 (15)	88 (1.2)	54–127	66–181
TSH (mUI/L)		1.8 (0.82)	1.5 (2.3)	0.09–3.7	1.8 (1.3)	1.6 (1.7)	0.25–10	0.35–4.5
freeT (pmol/L)	Men	165 (48)	159 (1.4)	91–254	226 (71)	212 (1.5)	30–446	223–915
	Women	8.0 (3.9)	7.1 (1.9)	3.0–12	12 (9.2)	8.9 (2.1)	0.20–1.7	<= 25
totalT (nmol/L)	Men	10 (4.6)	9.7 (1.5)	5.7–19	12 (4.5)	11 (1.7)	0.98–24	5.7–26
	Women	0.70 (0.26)	0.66 (1.5)	0.40–1.0	0.76 (0.42)	0.65 (1.8)	0.20–1.7	0.10–1.6
FSH (UI/L)	Men	5.4 (3.9)	4.3 (2.1)	1.2–15	5.7 (4.6)	4.6 (1.9)	0.50–35	1.0–18
LH (UI/L)	Men	4.4 (4.2)	2.8 (3.1)	0.20–14	5.5 (2.5)	5.0 (1.6)	0.50–17	2.0–12
E2[c] (pmol/L)	Men	71 (40)	62 (1.7)	ND–114	91 (38)	85 (1.5)	ND–165	95–223
Serum polybrominated diphenyl ethers (ng/g lipids) [c,d]								
BDE47		13 (21)	6.6 (3.1)	ND–115	12 (35)	3.8 (4.5)	ND–250	
BDE153		12 (16)	6.9 (2.8)	ND–60	8.0 (11)	4.6 (2.8)	ND–46	
BDE209		3.0 (4.1)	1.7 (2.8)	ND–8.6	32 (44)	18 (2.8)	ND–101	
Urinary organophosphate ester metabolites (ng/ml) [c,e]								
DPhP		1.2 (0.94)	0.95 (2.0)	0.24–2.5	2.5 (2.9)	1.7 (2.5)	ND–19	
BCiPHiPP		4.1 (15)	1.1 (5.2)	ND–17	3.0 (4.6)	1.7 (3.0)	ND–56	
BCiPCEP		1.1 (4.0)	0.28 (5.1)	ND–3.2	1.0 (1.9)	0.47 (3.4)	ND–24	
pOH-DPhP		0.093 (0.19)	0.041 (3.6)	ND–0.25	0.15 (0.22)	0.089 (2.9)	ND–0.61	
BCECMP		0.56 (3.1)	0.098 (6.4)	ND–2.3	0.81 (2.2)	0.28 (4.3)	ND–5.0	
tb-DPhP		0.030 (0.070)	0.012 (3.9)	ND–0.16	0.032 (0.027)	0.024 (2.1)	ND–0.21	
BDCiPP		1.6 (4.7)	0.5 (4.5)	ND–3.8	1.3 (2.8)	0.55 (3.7)	ND–7.4	

	Commercial recycling (n=15)			E-recycling (n=85[b])			
	AM (SD)	**GM (GSD)**	**Range**	**AM (SD)**	**GM (GSD)**	**Range**	
o-iPr-DPhP	0.018 (0.009)	0.016 (1.6)	ND–0.35	0.030 (0.034)	0.02 (2.5)	ND–0.18	
BCEHEP	0.043 (0.046)	0.028 (2.4)	ND–0.12	0.075 (0.048)	0.048 (2.6)	ND–0.79	
Blood metals (µg/l)							BEI®
Lead	20 (21)	14 (2.4)	ND-56	32 (42)	20 (2.7)	ND-137	200
Cadmium	1.5 (3.0)	0.66 (3.5)	.10 - 8.5	0.90 (1.7)	0.43 (3.4)	ND-4.4	5

[a] for men and women combined unless specified

[b] n=88 for OPE values

[c] Because of values below the limit of detection, results are calculated with a Bayesian model fit using a Monte Carlo Markov Chain engine (www.expostats.ca)

[d] Concentrations standardized on total blood lipids

[e] Concentrations standardized on urine specific gravity

Abbreviations: AM: arithmetic mean; SD: standard deviation; GM: geometric mean; GSD: geometric standard deviation; BEI: Biological exposure indices; freeT3: free triiodothyronine; totalT3: total triiodothyronine; freeT4: free thyroxine; totalT4: total thyroxine; TSH: thyroid-stimulating hormone; freeT: free testosterone; totalT: total testosterone; FSH: follicle stimulating hormone; LH: luteinizing hormone; E2: estradiol; ND: below detection limit.

The score plots for the principal component analyses in both types of facility are displayed in Figure 1 A and B. These plots illustrate the contribution of each biomarker to principal components one and two, which represent respectively 18% and 14% of the total variance for the e-recycling group, and 42% and 22% for the commercial recycling group. Detailed eigenvalues, proportion of explained variance, cumulative variance and biomarker loadings in each of the components are presented in Supplementary Table 4 for the two recycling groups. In e-recycling (Figure 1A), component 1 showed positive loadings (eigenvalue above |0.3|) by BCECMP, BCEHEP, DPhP and pOH-DPhP. Component 2 showed mainly positive loadings of BDE209 and Pb, and negative loadings of o-iPr-DPhP and Cd. In commercial recycling (Figure 1B), components 1 and 2 were represented entirely by OPE metabolites.

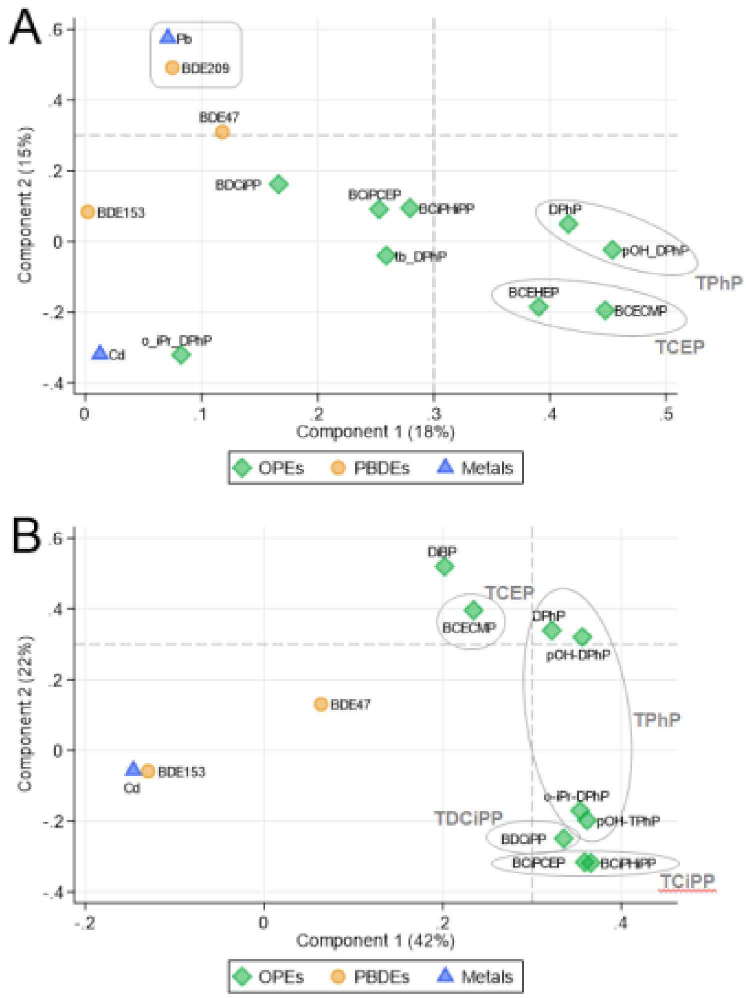

Figure 6.1 Principal component analysis. Loading plots for components 1 and 2 for A) E-recycling B) Commercial recycling. Gray rectangle shows the important loading of Pb and BDE209 on component 2 in e-recycling. Gray circles and text indicate parent compounds associated with OPE metabolites.

6.4.3. Hormonal concentrations and associations with flame retardants

Few participants had hormone values outside of the normal laboratory range (listed in Table 3), except for E2 for which 49 men had values below 95 pmol/L. Figures 2A to 2D show the percent change in hormone and ratios levels for a 2-fold increase in flame retardant concentrations. Regression coefficients and coefficients of determination of the models (R^2) can be found in supplementary tables 5 to 8. There were no statistically significant associations between any flame retardant and TSH (fig. 2B) or totalT3 (fig. 2A) levels in both men and women. The associations between flame retardants and most hormone levels were in the same direction for men and women. In women, a significant reduction in freeT3 (fig. 2A) was found in association with higher plasma BDE153 and BDE209 levels (-10%, 95% confidence interval (CI): -17, -3.2; and -3.5%, 95% CI: -6.6, -0.35), and with higher urinary tb-DPhP levels (-9.9%, 95% CI: -16, -3.5). In men, totalT4 (fig. 2A) was increased with BDE209 plasma levels (3.1%, 95% CI: 0.07, 6.1) and freeT4 (fig. 2A) was decreased (-4.1%, 95% CI: -7.9, -0.01) with urinary tb-DPhP levels. The ratio FreeT3/totalT3 (fig. 2D) was decreased with plasma BDE209 concentrations (-3.1%, 95% CI: -5.4, -0.69) and with urinary tb-DPhP levels (-5.7%, 95% CI: -10, -1.2), and freeT4/freeT3 (fig. 2D) was decreased with plasma BDE47 (-2.7%, 95% CI: -4.9, -0.42), with urinary tb-DPhP (-3.9%, 95% CI: -7.6, -0.14), and with urinary BDCiPP levels (-2.5%, 95% CI: -4.9, -0.14).

There were no statistically significant associations between FRs and testosterone levels or ratios in women. In men, FSH (fig. 2B) was decreased with higher urinary BCiPHiPP levels (-10%, 95% CI: -18, -1.1) and totalT (fig. 2C) was considerably decreased with higher urinary tb-DPhP levels (-18%, 95% CI: -29, -4.7). Likewise, freeT (fig. 2C) was decreased with higher urinary tb-DPhP (-18%, 95% CI: -27, -6.9). As for E2, it was increased by 16% (95% CI: 4.5, 30) with an increase in urinary o-iPr-DPhP concentration. The freeT/E2 (fig. 2D) ratio was decreased in association with higher urinary tb-DPhP (-13%, 95% CI: -25, 0.70).

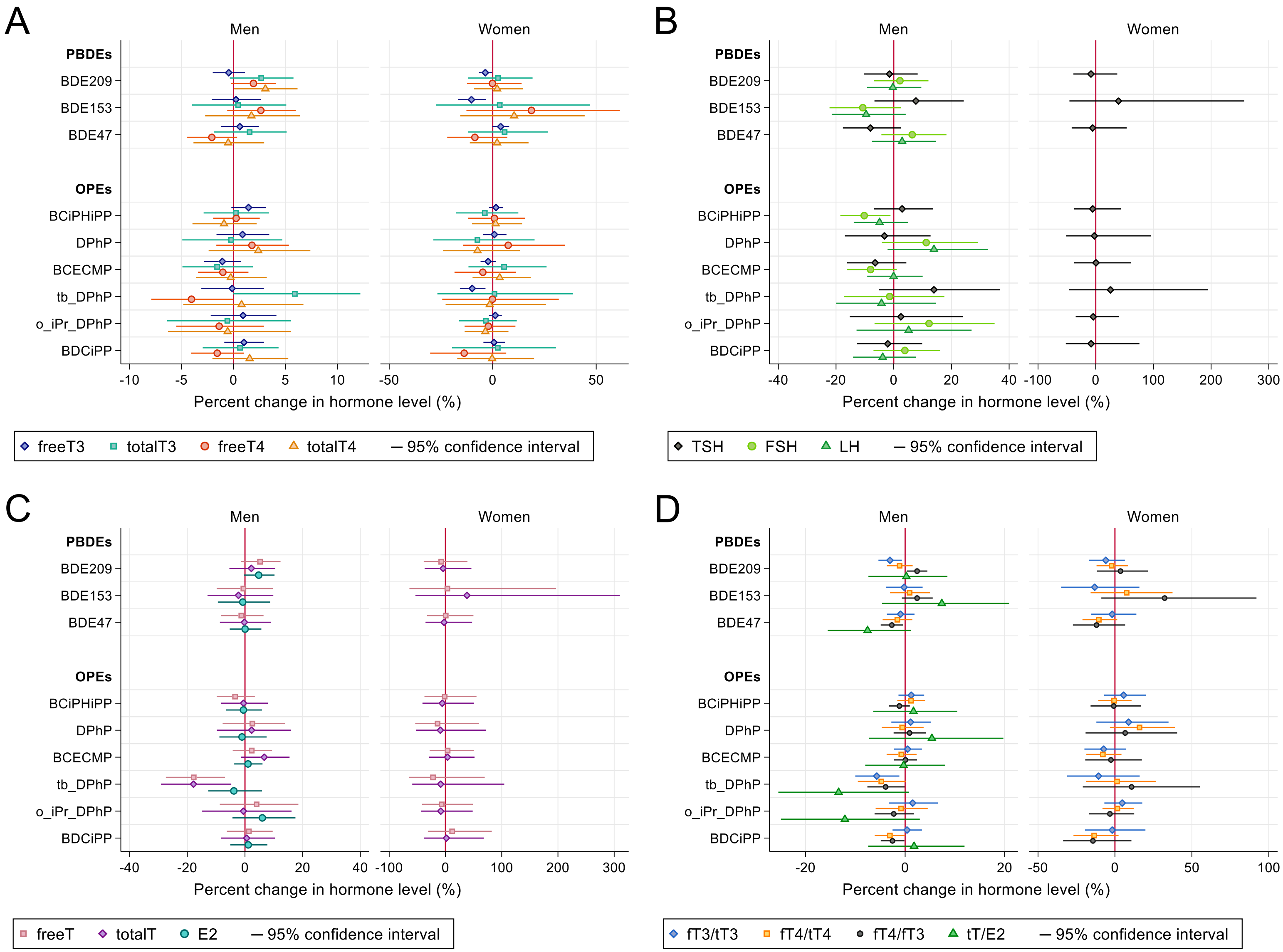
A
Men
Women
PBDEs
BDE209
BDE153
BDE47
OPEs
BCiPHiPP
DPhP
BCECMP
tb_DPhP
o_iPr_DPhP
BDCiPP
Percent change in hormone level (%)
freeT3 totalT3 freeT4 totalT4 — 95% confidence interval
B
TSH FSH LH — 95% confidence interval
C
freeT totalT E2 — 95% confidence interval
D
fT3/tT3 fT4/tT4 fT4/fT3 tT/E2 — 95% confidence interval

Figure 6.2. Percent change, for each two-fold increase in flame retardant concentration in A) thyroid hormones freeT3, totalT3, freeT4 and totalT4, B) hormones TSH, FSH and LH, C) sex hormones freeT, totalT and Estradiol, and D) Hormone levels' ratios. Models include all above-listed flame retardants, and are adjusted for blood cadmium and lead (µg/l), age (years, continuous), smoking status (yes/no) and body mass index (kg/m²). Men: n=74 for thyroid hormones, n=76 for sex hormones; women, n=19 for thyroid hormones, n=23 for sex hormones. Models excluded individuals with thyroid, gonad or pituitary diseases. PBDEs in blood [ng/g lipids]; OPE metabolites in urine [ng/ml]. See Table 1 notes for abbreviations.

6.5. Discussion

6.5.1. Flame retardants exposure

Our study is the first to report on biomarkers of exposure (i.e. biological concentrations) of flame retardants and metals in a Canadian population of e-recycling and commercial recycling workers. We found high detection frequencies for several biomarkers of exposure to FRs, as well as to metals, showing an important co-exposure pattern. The geometric mean concentration of BDE209 was 10 times higher in e-recycling than in our comparison group, and OPE metabolite concentrations were 1.1 to 2.9 times higher. Such differences suggest an occupational exposure to BDE209 and OPEs in e-recycling. In North American adults, BDE209 was reported in geometric mean concentrations from 1.4 to 3.2 ng/g lipids, which is close to what we measured in our comparison group (Rawn et al. 2014; Sjodin et al. 2019; Wu et al. 2015). On the other hand, BDE47 was previously detected in higher concentrations in the general adult working population (geometric mean [GM] US: 20.9 ng/g lipids; Canada: 11.4 ng/g lipids) (Gravel et al. 2018) than in both of our groups, but this population data is over ten years old and a decline in the background levels might have happened since (Ma et al. 2013). Additionally, the few North American studies that measured OPE urinary metabolites in the general population found concentrations that were similar to or higher than what was measured in our study (GM DPhP: 1.7 ng/ml; GM BDCiPP: 0.55 ng/ml). For instance, Yang et al. (2019) measured an unadjusted urinary DPhP GM of 12 ng/ml and BDCiPP of 0.74 ng/ml in Canadian women, and Hoffman et al. (2017a) measured specific gravity-adjusted GM DPhP levels of 1.5 ng/ml and BDCiPP levels of 1.3 ng/ml in US men and women.

Compared to population data, it appears that our measures of PBDE congeners in serum and of OPE urinary metabolites did not indicate a high occupational exposure, except for BDE209. BDE209 levels in the e-recycling group are comparable to reports of workers in cable manufacturing (GM: 22 ng/g lipids) and in rubber manufacturing (GM: 21 ng/g lipids) (Thuresson et al. 2005), and are higher than other measures in e-recycling workers in high-income countries (medians: 0.089 ng/g wet weight in Eguchi et al. (2012), 4.8 ng/g lipid in Sjodin et al. (1999) and 1.9-2.9 ng/g lipid in Thuresson et al. (2006a)). There are a few studies that measured urinary OPE metabolites in working populations presumably exposed to those FRs. DPhP levels measured in our study were similar to those of flight crew (unadjusted median: 1.1 ng/ml in Schindler et al. (2013)), and our BDCiPP levels were much lower than in office workers (specific gravity-adjusted GM: 408 ng/ml in Carignan et al. (2013)). However, it was also noted by Saillenfait et al. (2018) that OPE metabolites are subject to many factors affecting their concentration in urine, which means that we cannot exclude that unmeasured factors could have impacted our results, such as the timing of sampling or the consumption of certain foods during the day.

6.5.2. Exposure patterns

We used a PCA in order to visualize and compare exposure patterns to FRs detected in more than 40% of samples in e-recycling and in the comparison group. The clusters of biomarkers that score higher in the first component in both groups represent concomitant exposures to OPEs, while component 2 in e-recycling represents mainly concomitant exposures to Pb and BDE209 (Figure 2A). Component 2 in e-recycling is coherent with exposures to contaminants found in cathode ray tube TVs, which are commonly treated in this type of industry (Abbasi et al. 2016; Lecler et al. 2015). The OPE metabolite patterns in our PCA are coherent with OPE patterns that were previously observed in home dust, and the differences observed between our groups might not be large enough to differentiate between occupational and background exposures (Bergh et al. 2011; Harrad et al. 2016). We chose the 40% cut off because PCA is known to perform better in fuller datasets (Farnham et al. 2002), but in our case this entails a different set of included variables for our two groups, as some biomarkers had detection rates lower than 40% in one or the other group.

6.5.3. Association with hormone levels

Our population did not have hormonal disruptions of clinical significance, except for E2 for which about half of the men had levels below the laboratory normal range. As the subjects included in the E2 analyses were excluded if they reported gonadal problems, and because none of the covariables were associated with the E2 levels, this high proportion of values outside of normal range could be attributed simply to a restrictive laboratory range or to other unmeasured factors such as diurnal variations. Some congeners of PBDEs and OPE metabolites were associated with freeT3, totalT4, and freeT4 variations, and with certain hormone ratios. Associations between thyroid hormones and PBDEs or OPEs have been reported in the literature, but results are inconsistent. PBDEs have a molecular structure similar to that of thyroid hormones, and some of their hydroxylated metabolites have been shown in animal models to be competitive inhibitors of thyroid hormone binding to their receptors, as well as inhibitors of thyroid hormone receptor gene expression (Wiseman et al. 2011). While the evidence is still scarce for other flame retardants, some OPEs such as TPhP and TDCiPP have been observed *in vitro* to increase freeT4 binding to its transport proteins, possibly through allosteric activation (Hill et al. 2018). The thyroid hormone equilibrium is finely regulated and a disruption in T3 or T4 binding to their receptors or transport proteins can manifest itself in several ways, especially in the presence of molecules acting in opposite fashions (Koulouri et al. 2013). Hormone ratios, albeit rarely used, present an interesting metric when studying the effect of potential endocrine disruptors (Sollberger and Ehlert 2016). Changes in freeT3/totalT3 and freeT4/totalT4 ratios can reflect a toxicity mechanism involving transport proteins, while freeT4/freeT3 can reflect an action on deiodinases which are required for the conversion of T4 into T3 (Feldt-Rasmussen and Rasmussen 2007). Such effects have indeed been observed *in vivo* with a combination of OPE FRs (Liu et al. 2019), as well as with various endocrine disruptors, such as PCBs, pesticides, metals and flame retardants (Boas et al. 2012; Iavicoli et al. 2009; Zoeller 2007). Our population of e-recycling workers could hence present some thyroid hormone disruptions through several mechanisms simultaneously.

We observed associations between sex hormones and biomarkers of exposure to FRs, especially with OPEs. To our knowledge, this is the first study to show significant associations between OPE metabolites and sex hormones and their ratios, in adults. The effect of exposure to FRs on sex hormones has been less studied than on thyroid hormones, but *in vitro* and *in vivo* data on organophosphorus pesticides and flame retardants have suggested an alteration of steroid hormones synthesis (Androutsopoulos et al. 2013; Schang et al. 2016). Evidence is increasing on an antagonist action of OPEs on estrogen/androgen receptors in animals and in human cells, as well as an effect of PBDEs on semen quality in men and animals possibly through a reduction in thyroid hormones and testosterone (Albert et al. 2018; Dishaw et al. 2014; Sarkar et al. 2016). Moreover, since testosterone can be converted to E2 by aromatases (Bolander 2004), it is not excluded that this process could be enhanced in the presence of multiple OPE metabolites as some upregulation of aromatases have been noticed with other endocrine disruptors (De Coster and van Larebeke 2012).

The mechanisms of hormonal disruption by PBDEs and OPEs are complex, not fully elucidated, and do not necessarily display a classic monotonic toxicity response (Boas et al. 2012; Dishaw et al. 2014; Gore et al. 2015; Zhao et al. 2015). While it is difficult to find mechanistic explanations for these associations and to grasp the potential physiological effects with the current state of knowledge, the strength and the magnitude of the associations that we observed warrant more research on the effect of FRs on thyroid and reproductive hormones in adults, and its consequences.

6.5.4. Limitations and strengths

Our study presents certain limitations. We believe that our sample gives a fair representation of the e-recycling industry in the province of Québec, namely nonprofit, for-profit, and "trade school" companies, but cannot conclude on the representativeness of the results for all of Canada. The cross-sectional design does not allow the assessment of temporality between exposure and outcomes. Blood samples were taken in the afternoon, which can influence the measured levels of hormones that are subjected to diurnal variations (Brambilla et al. 2009; Fisher 1996). Several thyroid and sex hormones tend to decrease over the day, but the blood sampling was performed between 4 p.m. and 6 p.m. for most participants, which should not have impacted on the associations. We used end-of-shift spot urine samples only, which may underestimate exposure (LaKind et al. 2019), along with an unknown non-occupational exposure (diet, house dust, etc.). Moreover, hormone concentrations were determined by immunoassay techniques that are routinely used in clinical settings, but can be criticized as not being precise enough (Welsh and Soldin 2016). Our sample size was too small to allow the inclusion of ethnicity as a covariable in regression analyses or to highlight significant associations in subsamples of men or women. Considering the multiple comparisons performed and the number of confidence intervals calculated across the regressions (multiple testing), we cannot exclude that some of the statistically significant associations do in fact reflect random chance. Our analyses on hormone ratios, as well as the inclusion of several analytes, allowed the exploration of the mechanisms and combined effects of multiple contaminants on hormone levels in workers. However, it is unknown whether the percent changes that we observed in hormone levels have any clinical impact. We believe that our study contributes in expanding the knowledge on exposure to flame retardants in workers, and on endocrine effects that can be observed in a highly exposed sub-population.

6.6. Conclusion

E-recycling workers can be exposed to high concentrations of flame retardants, some of which were associated with endocrine variations in our dataset. Reproductive and thyroid function in men and women require an endocrine equilibrium that can be affected by a combination of exposures such as flame retardants and metals. Our study results should foster an interest on the association between hormones and various chemical groups of flame retardants. Finally, although our results are not all conclusive and need replication, they suggest that prudent avoidance could be applied in risk management of flame retardants in the workplace.

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6.9. Supplementary material

6.9.1. Methodological details

Urine and blood specimen collection

Urine samples for OPE analyses were collected in 500 mL polyethylene bottles (Fisher Scientific no. 03-415-502); they were transported on ice to the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) laboratory where they were transferred into 50 ml polyethylene centrifugation tubes (Corning™, Lowell, MA) and frozen at -70°C. Urine samples for Hg were collected in 125 mL polyethylene bottles (Nalgene) at the end of the second sampling day; they were transported on ice to the IRSST laboratory where they were kept at 4°C until their analysis.

A registered nurse proceeded to the blood draw from a cubital vein for all participants after the second day work shift. Vacuum sealed blood collection tubes (BD Vacutainer®, Becton Dickinson, Franklin Lakes, NJ) were used to collect blood for analyses of Cd (royal blue top tubes for trace elements coated with silicone), Pb and PBDEs (lavender top tubes coated with K2EDTA), and hormones (gold top tubes coated with silicone and containing a polymer gel for serum separation). Blood samples for Cd, Pb were transported at room temperature to the IRSST laboratory where they were stored at 4°C until their analysis. The tubes for PBDE analysis were transported at room temperature to the IRSST laboratory where they were centrifuged within 4h of collection for isolation of the serum. Serum was then transferred into 2 ml silane pre-treated chromatography vials (Supelco® Analytical, Pa, USA), then frozen at -20°C.. The blood samples for hormones analyses were centrifuged onsite before being taken to the laboratory at room temperature for analysis.

Laboratory analysis

Flame retardants and metals

The blood samples for Cd were sent on ice to the Centre de toxicologie du Québec (CTQ; Institut national de santé publique du Québec, Québec City, Canada) for analysis by inductively coupled plasma mass spectrometry with Dynamic Reaction Cell II (ICP-MS, DRC II; Perkin-Elmer, Wellesley, MA, USA). The blood samples for Pb analyses were also kept at 4°C before analysis at the IRSST by graphite furnace atomic absorption spectrometry with Zeeman background correction (GFAAS; model 240Z, Agilent Technologies Inc.; Mississauga, Canada) (Gagné et al. 2018b). Serum samples for PBDE analyses were sent on ice to the CTQ where the PBDE congeners listed in Table 6.1 were analyzed on an Agilent 6890 Network gas chromatograph (GC) equipped with an Agilent 5975 mass spectrometer (MS) (Agilent Technologies Inc.; Mississauga, Canada). Blood lipids (sum of triglycerides and total cholesterol) were analyzed at the CTQ.

Urinary mercury levels were determined at the IRSST by cold vapour atomic absorption spectroscopy (FIMS-100; Perkin-Elmer, Wellesley, MA, USA) (Gagné et al. 2018a). Urine samples for OPE metabolites were sent on dry ice to the CTQ where the metabolites listed in Table 6.1 were analyzed by Ultra Performance Liquid Chromatography (UPLC Acquity, Waters, Milford, MA) with a tandem mass spectrometer (MS/MS Xevo TQ-XS, Waters, Milford, MA).

Urine specific gravity was measured using a digital handheld refractometer in the respective laboratories for each analysis. Urinary creatinine was analyzed at IRSST by a spectrometric method based on Jaffe's reaction with a detection limit of 0.06 mmol/L (Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) 1996).

Both the CTQ and IRSST laboratories have the ISO/CEI 17025 accreditation for their respective analyses, but the method for analysis of urinary metabolites of OPEs is pending accreditation at the CTQ and is hence described in detail as follows:

Chemical analyses of organophosphate flame retardants in urine

The 15 following organophosphate flame retardant metabolites were analyzed in urine samples: BCiPCEP, DiPP, DPhP, pOH-TPhP, pOH-DPhP, BBOEP, BCECMP, BCEHEP, BDCiPP, DBP, DiBP, BCiPHiPP, o-iPr-DPhP, p-iPr-DPhP, tb-DPhP. Analysis was performed at the Centre de toxicologie du Québec (CTQ) of the Institut national de santé publique du Québec (INSPQ).

Extraction

DiPP, DPhP and pOH-DPhP were analyzed in a separate run from the other metabolites. Volumes of 250 µL of urine were enriched with labelled internal standards (DPhP-13C2 and pOH-DPhP-d5) and hydrolyzed with 250 µL of β-glucuronidase enzyme solution 1 % (from E.coli K12, Roche Diagnostics, Hoffmann-La Roche Limited; Mississauga, Ontario, Canada) in an acetate buffer 1 M for 90 minutes at 37°C. The samples were then acidified with formic acid 5 % before solid phase extraction (SPE) with SiliaPrepX WAX cartridges (3 mL, 100 mg; SiliCycle, Quebec, Canada). The SPE cartridges were conditioned beforehand with NH_4OH 0.5 %, followed by formic acid 1 %. They were then washed with water and methanol, and elution of the analytes was done with 2 mL of NH_4OH 0.5 % in methanol. The extracts were evaporated completely and dissolved in 250 µL of acetonitrile 5 % solution.

For analysis of the other metabolites (BBOEP, BCECMP, BCEHEP, BCiPCEP, BDCiPP, DBP, DiBP, pOH-TPhP, BCiPHiPP, o-iPr-DPhP, p-iPr-DPhP, tb-DPhP), the 250 µL urine samples were spiked with labelled internal standards BDCiPP-d12, BDBrPrP-d10, BDCliPrP-d10, BmTyP-d14, DiBP-d14, DPhP-13C2, 4-MLBF-13C4, and 4-methylumbelliferone glucuronide. The samples were then hydrolyzed with 250 µL of β-glucuronidase enzyme solution 1 % in an acetate buffer 1 M during 90 minutes at 37°C. Afterwards, they were acidified with hydrochloric acid 10 % and extracted with ethyl acetate (3 mL) using a liquid-liquid extraction. The extracts were evaporated completely and dissolved in 100 µL of acetonitrile 40 % solution.

Analysis

The extracts for both batches of metabolites were analyzed by Ultra Performance Liquid Chromatography (UPLC Waters Acquity) with a tandem mass spectrometer (MS/MS Waters Xevo TQ-XS) (Waters; Milford, MA, USA) in the Multiple Reaction Monitoring (MRM) mode with an electrospray ion source in the negative and positive modes. For the first 3 analytes, BEH C18 100 mm x 2.1 mm x 1.7 µm (Waters; Milford, MA, USA) columns were used, and HSS T3 150 mm x 2.1 mm x 1.8 µm (Waters; Milford, MA, USA) for the others. In both cases, the column temperature was set to 50°C while the autosampler was set to 4°C and the injection volumes were 5 µL in partial loop (needle overfill mode). The mobile phase was a gradient of formic acid 0.1 % solution (100 %) to a mixture of acetonitrile:H2O with formic acid 0.1 % (95:5) in 14.0 minutes with a flow rate of 0.45 mL/minute.

QA/QC

The limits of detection reported (LOD) ranged between 0.0093 and 0.2 ng/mL for the first three analytes and between 0.015 and 0.17 µg/L for the others. The LOD was assessed on a urine sample with a base level of OPE metabolites and was spiked with analytes to reach a concentration ranging from 4 to 10 times the estimated LOD (10 replicates). The standard deviation obtained was then multiplied by 3 to provide the LOD. The intra-day precision was between 3.4 to 10 % for the first 3 analytes and between 3.6 to 11 % for the rest.

The internal reference materials used were in-house prepared in urine, with a second source of standard when available, by the Centre de toxicologie du Québec (CTQ), Institut National de santé publique du Québec (INSPQ).

Hormones

Hormone analyses were overseen by a privately owned clinical laboratory following standard clinical procedures. For both men and women, total thyroxine (totalT4) was analyzed using a Roche Diagnostics Electrochemiluminescence (ECL) assay on a Cobas 6000 analyser (Roche Diagnostics GmbH, Germany), and freeT4, total triiodothyronine (totalT3) and freeT3 were analyzed using a Siemens Chemiluminescence Competitive assay on a Centaur XP system (Siemens Healthcare GmbH, Germany). Again for both men and women, thyroid-stimulating hormone (TSH), follicle stimulating hormone (FSH) and luteinizing hormone (LH) were analyzed using a Siemens Chemiluminescence Sandwich assay on a Centaur XP system (Siemens Healthcare GmbH, Germany). For men only, estradiol (E2) was analyzed using a Roche Diagnostics ECL assay on a e411 analyser (Roche Diagnostics GmbH, Germany), and free testosterone (freeT) was calculated using the Vermeulen Equation (Vermeulen et al. 1999) based on the analysis of sex hormone binding globuline (SHBG) and total testosterone (totalT) using a Beckman Chemiluminescence Sandwich assay on a Beckman Coulter DXI system (Beckman Coulter Inc, USA). For women, the same equation was used, but based on the analysis of SHBG using a Chemiluminescence Assay on an Immulite XPI 2000 system

(Siemens Healthcare GmbH, Germany), with totalT on an Agilent 1200 Liquid Chromatograph (Agilent Technologies, USA) coupled with a Sciex 4000 QTrap Mass Spectrophotometer (AB Sciex, Canada).

6.9.2. Supplementary tables

Table S6.1 Summary of some statistically significant associations* between PBDEs or OPE flame retardant exposure and thyroid and reproductive hormone levels in adults.

						Thyroid hormones					Sex hormones					
Population	**N**	**Country**	**Study design**	**Exposure matrix**	**FR sampled**	**fT3**	**TT3**	**fT4**	**TT4**	**TSH**	**fT**	**TT**	**FSH**	**LH**	**E2**	**Reference**
Workers																
E-recycling workers	14	Sweden	L	Plasma	PBDEs		—[a]	—		—						Julander et al. (2005a)
E-recycling workers (33m 36w)	79	China	CS	Serum	PBDEs	—	BDE47 ↑ BDE66 ↑ BDE85 ↑	—	BDE66 ↑ BDE85 ↑	—						Zheng et al. (2017)
E-recycling workers (32m 45w) and residents from a rural area (12m 22w)	111	Vietnam	CS	Serum	PBDEs	—	—	—	—	—						Eguchi et al. (2015)
People working in (236) or living near (89) e-recycling facilities, people from green plantation (117)	442	China	CS	Air (ambient) and soil	PBDEs	—	—	—	BDE126 ↑ BDE205 ↑	—						Wang et al. (2010)

						Thyroid hormones					Sex hormones					
Population	**N**	**Country**	**Study design**	**Exposure matrix**	**FR sampled**	**fT3**	**TT3**	**fT4**	**TT4**	**TSH**	**fT**	**TT**	**FSH**	**LH**	**E2**	**Reference**
Local residents from an e-recycling region (54) and another region (58)	112	China	CS	Serum	PBDEs						BDE47↑ BDE100↑ BDE153↑ BDE183↑ BDE204↑		—	BDE85↑ BDE99↑ BDE100↑	BDE47↑ BDE209↑	Guo et al. (2018b)
Office workers (26m 25w)	51	United States	L	Serum	PBDEs		—	—	BDE47 ↓ BDE99 ↓ BDE100 ↓	—						Makey et al. (2016a)
Office workers (26m 26w)	52	United States	L	Urine	OPEs		—	—	DPhP ↑ (w)	—						Preston et al. (2017)
Office workers (27m)	27	United States	L	Serum	PBDEs						—	—	BDE47 ↑ (>40 y.o.) BDE100 ↑ (>40 y.o.) BDE153 ↑ (>40 y.o.)	—		Makey et al. (2016b)
General population																
Healthy men	153	Canada	CS	Hair	PBDEs	—		—		BDE47 ↓		—		—		Albert et al. (2018)
Men 18-54 years old	62	United States	CS	Dust from vacuum bags at home	PBDEs		PentaBDE ↑	PentaBDE ↑ OctaBDE ↑		OctaBDE ↑	OctaBDE ↑ DecaBDE ↓		PentaBDE ↓	OctaBDE ↑	PentaBDE ↑	Johnson et al. (2013)
General population (60m 64w)	124	China	CS	Serum	PBDEs		BDE17 ↓ BDE28 ↓ BDE47 ↓ BDE99 ↑ BDE153 ↓ BDE183 ↓ BDE209 ↑	—		BDE17 ↑ BDE28 ↑ BDE47 ↑ BDE99 ↓ BDE183 ↑						Huang et al. (2014)

Population	N	Country	Study design	Exposure matrix	FR sampled	Thyroid hormones					Sex hormones					Reference
						fT3	TT3	fT4	TT4	TSH	fT	TT	FSH	LH	E2	
Remote population of St. Lawrence Island Yupik (38m 36f)	85	United States	CS	Serum	PBDEs	BDE28/33 ↑ BDE47 ↑ BDE100 ↑	BDE153 ↓	—	—	BDE28/33 ↑ BDE47 ↑ BDE100 ↑						Byrne et al. (2018)
Inuit population (245m 378w)	623	Canada	CS	Plasma	PBDEs		BDE47 ↑	—		—						Dallaire et al. (2009)
Men anglers	36	Canada	CS	Plasma	PBDEs		—	—	—	—						Bloom et al. (2008)
Men fish consumers	405	United States	CS	Serum	PBDEs	—	—	BDE47 ↑ ΣPBDE ↑	ΣPBDE ↑	BDE47 ↓						Turyk et al. (2008)
Men; andrology clinic	33	United States	CS	Urine	OPEs	—	BDCiPP ↑	—	—	BDCiPP ↑		—	—	—	—	Meeker et al. (2013a)
Men; fertility clinic	24	United States	CS	Dust from vacuum bags at home	PBDEs		—	BDE47 ↑ BDE99 ↑ BDE100 ↑		—		—	BDE47 ↓ BDE99 ↓ BDE100 ↓	BDE47 ↓ BDE99 ↓ BDE100 ↓	—	Meeker et al. (2009)
Men; fertility clinic	52	Canada	CS	Serum	PBDEs	—	—	—	BDE47 ↓ BDE99 ↓ ΣPBDE ↓	—						Abdelouahab et al. (2011)
Men; general population	110	Sweden, Latvia	CS	Plasma	PBDEs	—	—	—	—	BDE47 ↓	—	—	—	—	—	Hagmar et al. (2001)

Population	N	Country	Study design	Exposure matrix	FR sampled	Thyroid hormones					Sex hormones					Reference
						fT3	TT3	fT4	TT4	TSH	fT	TT	FSH	LH	E2	
Men; spouses of pregnant women	299	Greenland, Poland, Ukraine	CS	Serum	PBDEs								—	—	—	Toft et al. (2014)
Pregnant women																
Pregnant women	270	United States	CS	Plasma	PBDEs			—	—	BDE28 ↓ BDE47 ↓ BDE99 ↓ BDE100 ↓ BDE153 ↓						Chevrier et al. (2010)
Pregnant women	125	China	CS	Serum	PBDEs						—		BDE47 ↓ BDE100 ↓ ΣPBDE ↓	—	—	Gao et al. (2016)
Pregnant women	105	Korea	CS	Serum	PBDEs	ΣPBDE ↓	BDE47 ↓ ΣPBDE ↓	ΣPBDE ↑	—	—						Kim et al. (2013)
Pregnant women	137	United States	CS	Serum	PBDEs	—	—	BDE47 ↑ BDE154 ↑ ΣPBDE ↑	BDE47 ↑ BDE99 ↑ BDE100 ↑ ΣPBDE ↑	—						Stapleton et al. (2011)

* Results compiled for adjusted models
[a] Dash "—" indicates no significant effect on the hormone tested.
Abbreviations: CS: Cross-sectional; L: Longitudinal; PBDEs: polybrominated diphenyl ethers; OPEs: organophosphate esters; fT3: free triiodothyronine; TT3: total triiodothyronine; fT4: free thyroxine; TT4: Total thyroxine; TSH: thyroid-stimulating hormone; fT: free testosterone; TT: total testosterone; FSH: follicle stimulating hormone; LH: luteinizing hormone; E2: estradiol

Table S6.2. Spearman's rank correlations between biomarker concentrations of flame retardants and metals detected in more than 20% of biological samples in e-recycling.

	BDE47	BDE153	BDE183	BDE209	BBOEP	BCECMP	BCEHEP	BCiPCEP	BDCiPP	DBP	DiBP	DPhP	BCiPHiPP	oiPrDPhP	pOH-DPhP	pOH-TPhP	tbDPhP	Cadmium	Lead	Mercury
BDE47	1																			
BDE153	**.23**	1																		
BDE183	**.31**	**.26**	1																	
BDE209	.11	.05	**.30**	1																
BBOEP	.10	.07	.03	-.07	1															
BCECMP	**.26**	.14	.05	.10	**.34**	1														
BCEHEP	**.24**	.08	.05	.09	**.44**	**.78**	1													
BCiPCEP	.20	.07	.04	**.23**	**.25**	**.49**	**.51**	1												
BDCiPP	.03	.10	.11	.19	.18	**.36**	**.39**	**.59**	1											
DBP	.09	-.06	.05	**.25**	**.31**	**.46**	**.46**	**.39**	**.41**	1										
DiBP	.20	.04	**.23**	.04	**.37**	**.44**	**.49**	**.55**	**.48**	**.41**	1									
DPhP	**.32**	.05	.04	**.23**	**.35**	**.64**	**.58**	**.57**	**.46**	**.48**	**.49**	1								
BCiPHiPP	.16	.01	.06	.19	.16	**.46**	**.48**	**.94**	**.59**	**.40**	**.57**	**.52**	1							
o-iPr-DPhP	**.25**	.16	.02	-.01	**.52**	**.51**	**.45**	**.43**	**.28**	**.39**	**.38**	**.56**	**.35**	1						
pOH-DPhP	**.23**	-.04	.01	.08	**.38**	**.48**	**.58**	**.47**	**.41**	**.48**	**.49**	**.76**	**.44**	**.45**	1					
pOH-TPhP	.16	-.10	.08	.04	**.57**	**.30**	**.51**	**.36**	**.25**	**.42**	**.40**	**.52**	**.30**	**.40**	**.75**	1				
tb-DPhP	.13	.02	-.04	.04	**.24**	**.47**	**.47**	**.54**	**.54**	**.41**	**.57**	**.52**	**.56**	**.43**	**.42**	**.36**	1			
Cadmium	-.13	.03	-.01	.06	.10	**.27**	.18	.03	.00	**.32**	.01	-.01	.01	**.25**	.05	.11	-.02	1		
Lead	.08	-.05	**.31**	**.63**	**-.27**	.06	.04	**.26**	.18	**.23**	.21	.11	**.26**	-.17	.04	-.02	.07	.01	1	
Mercury	-.14	.03	-.19	-.10	.21	-.08	-.18	-.16	-.18	-.10	-.18	-.10	-.21	.15	-.10	-.05	-.05	.16	**-.24**	1

Strength of the correlation
- .00-.19 very weak
- .20-.39 weak
- .40-.59 moderate
- .60-.79 strong
- .80-1.0 very strong

Bold indicates p<0.05. See full names of biomarkers in Table 1 from the main article.

Table S6.3. Spearman's rank correlations between biomarker concentrations of flame retardants and metals detected in more than 20% of samples in commercial recycling.

	BDE47	BDE99	BDE100	BDE153	BDE209	BCECMP	BCEHEP	BCiPCEP	BDCiPP	DiBP	DPhP	BCiPHiPP	o-iPr-DPhP	pOH-DPhP	pOH-TPhP	tb-DPhP	Cadmium	Lead
BDE47	1																	
BDE99	**.71**	1																
BDE100	**.71**	**1**	1															
BDE153	.23	.31	.31	1														
BDE209	-.24	-.29	-.29	-.44	1													
BCECMP	.00	-.13	-.13	-.24	-.13	1												
BCEHEP	.31	-.04	-.04	.01	-.35	**.84**	1											
BCiPCEP	-.02	.10	.10	.22	-.26	.29	.29	1										
BDCiPP	.08	.13	.13	.11	-.24	**.53**	.36	**.75**	1									
DiBP	.08	.05	.05	.14	**-.53**	**.66**	**.63**	.29	.57	1								
DPhP	.24	.10	.10	.08	-.18	.57	.60	.48	.54	.76	1							
BCiPHiPP	-.05	.10	.10	.17	-.16	.32	.32	**.95**	**.63**	.29	.50	1						
o-iPr-DPhP	-.02	-.13	-.13	-.32	-.16	**.64**	**.54**	**.64**	**.62**	**.57**	**.60**	**.68**	1					
pOH-DPhP	.25	.17	.17	-.10	-.27	**.52**	.51	**.55**	**.54**	**.73**	**.87**	**.61**	**.77**	1				
pOH-TPhP	.27	.35	.35	.07	-.16	.38	.33	**.83**	**.82**	.46	**.69**	**.78**	**.63**	**.72**	1			
tb-DPhP	.16	.48	.48	.11	-.23	.12	.12	**.58**	.34	.15	.40	.51	.17	.37	**.65**	1		
Cadmium	.14	.49	.49	.07	.10	-.24	-.19	-.04	-.36	-.49	-.24	.03	-.44	-.29	-.02	.48	1	
Lead	-.05	.00	.00	.16	-.10	.26	.23	.45	.30	.19	.07	.46	.31	.18	.38	.28	-.10	1

Bold indicates p<0.05. See full names of biomarkers in Table 1 from the main article.

Table S6.4. Eigenvalues, variance explained, cumulative variance and loadings in the principal components for e-recycling workers and for commercial recycling workers.

Components	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14
E-recycling														
Eigenvalue	2.5	2.0	1.9	1.6	1.3	1.1	0.97	0.77	0.74	0.51	0.30	0.23	0.089	0.015
Variance explained (%)	18	15	14	11	9.2	7.6	6.9	5.5	5.3	3.6	2.1	1.6	0.6	0.1
Cumulative variance (%)	18	32	46	57	67	74	81	87	92	96	98	99	100	100
BDE47	0.118	0.309	0.193	-0.197	0.273	0.380	-0.080	0.257	-0.634	0.111	-0.248	-0.214	0.044	-0.023
BDE153	0.002	0.084	-0.004	-0.259	0.011	0.765	0.287	-0.044	0.473	0.100	0.101	0.107	0.028	0.013
BDE209	0.075	0.492	0.176	0.082	0.215	-0.222	0.244	-0.083	0.390	-0.348	-0.449	-0.276	0.035	-0.042
BCECMP	0.448	-0.195	0.173	-0.424	0.074	-0.135	0.054	0.001	0.045	-0.088	0.074	-0.062	-0.711	-0.004
BCEHEP	0.390	-0.185	0.162	-0.507	0.011	-0.195	-0.084	-0.021	0.074	-0.086	0.034	0.067	0.683	0.028
BCiPCEP	0.253	0.091	-0.631	-0.003	0.174	-0.006	0.019	0.036	-0.022	-0.042	-0.061	-0.010	-0.002	0.702
BCiPHiPP	0.280	0.094	-0.620	-0.003	0.144	-0.011	0.034	0.055	-0.015	-0.023	0.076	-0.022	0.036	-0.704
BDCiPP	0.166	0.162	-0.019	-0.035	-0.430	-0.144	0.648	-0.333	-0.297	0.337	-0.067	0.033	0.037	0.013
DPhP	0.416	0.050	0.161	0.401	-0.007	0.154	-0.194	-0.314	0.051	0.110	0.418	-0.529	0.083	0.052
o-iPr-DPhP	0.082	-0.321	0.106	0.269	0.443	0.164	0.297	-0.367	-0.273	-0.424	0.012	0.322	0.050	-0.018
pOH-DPhP	0.454	-0.024	0.114	0.333	-0.089	0.094	-0.288	0.007	0.150	0.314	-0.486	0.456	-0.048	-0.039
tb-DPhP	0.259	-0.040	0.072	0.263	-0.436	0.122	0.231	0.611	-0.055	-0.455	0.114	0.016	0.048	0.031
Cd	0.012	-0.319	0.097	0.189	0.440	-0.176	0.399	0.436	0.157	0.472	0.031	-0.157	0.084	0.016
Pb	0.071	0.575	0.172	0.030	0.224	-0.198	0.001	0.119	0.000	0.078	0.530	0.490	-0.026	0.050
Commerical recycling														
Eigenvalue	5.0	2.6	1.6	1.0	0.78	0.56	0.18	0.10	0.066	0.021	0.0084	0.0019		
Variance explained (%)	42	22	13	8.6	6.5	4.7	1.5	0.86	0.55	0.17	0.070	0.020		
Cumulative variance (%)	42	64	77	86	92	97	98	99	100	100	100	100		
BDE47	0.064	0.130	0.735	0.070	-0.160	-0.241	0.012	0.463	-0.188	0.003	0.047	0.314		
BDE153	-0.130	-0.059	0.128	0.819	0.414	0.289	0.178	0.015	0.020	0.064	0.031	-0.020		
BCECMP	0.234	0.396	-0.301	0.037	0.359	-0.280	-0.248	0.120	-0.194	0.494	0.344	0.114		
BCiPCEP	0.359	-0.316	-0.052	0.087	0.216	-0.141	-0.340	0.084	-0.217	0.031	-0.723	0.027		
BCiPHiPP	0.366	-0.318	-0.056	0.066	0.114	0.073	-0.388	0.128	0.132	-0.545	0.492	0.125		
BDCiPP	0.336	-0.249	-0.079	0.015	0.140	-0.536	0.675	0.046	0.058	-0.081	0.089	-0.194		
DiBP	0.202	0.520	-0.171	0.026	0.085	0.054	0.154	0.154	0.549	-0.261	-0.313	0.367		
DPhP	0.322	0.339	0.262	0.052	0.043	-0.014	0.038	-0.727	-0.331	-0.258	0.003	0.055		
o-iPr-DPhP	0.354	-0.171	-0.178	-0.125	-0.162	0.555	0.371	0.111	-0.327	0.203	0.052	0.405		
pOH-DPhP	0.356	0.320	0.098	-0.037	-0.059	0.327	-0.004	0.328	-0.071	-0.059	-0.025	-0.729		
pOH-TPhP	0.362	-0.198	0.348	-0.029	-0.084	0.090	-0.111	-0.270	0.580	0.516	0.062	-0.036		
Cd	-0.147	-0.057	0.285	-0.539	0.741	0.205	0.103	0.026	0.019	-0.041	-0.004	0.014		

Table S6.5. Coefficients and 95% confidence intervals in linear regression multivariable[a] models for thyroid hormones and their ratios in men. (N=74)

	ln(freeT3)	ln(totalT3)	ln(freeT4)	ln(totalT4)	ln(TSH)	ln(fT3/tT3)	ln(fT4/tT4)	ln(fT4/fT3)
ln(BDE209)	-0.007 [-0.029, 0.016]	0.038* [-0.005, 0.081]	0.027* [-0.003, 0.058]	0.044** [0.001, 0.086]	-0.021 [-0.158, 0.115]	-0.045** [-0.080, -0.010]	-0.016 [-0.054, 0.022]	0.034** [0.005, 0.063]
ln(BDE153)	0.003 [-0.031, 0.037]	0.006 [-0.059, 0.072]	0.038 [-0.009, 0.084]	0.025 [-0.040, 0.089]	0.107 [-0.100, 0.313]	-0.003 [-0.056, 0.050]	0.013 [-0.044, 0.070]	0.034 [-0.010, 0.078]
ln(BDE47)	0.009 [-0.017, 0.035]	0.022 [-0.028, 0.072]	-0.030* [-0.066, 0.005]	-0.007 [-0.057, 0.042]	-0.122 [-0.280, 0.036]	-0.013 [-0.054, 0.027]	-0.023 [-0.067, 0.021]	-0.039** [-0.073, -0.006]
ln(BCiPHiPP)	0.021* [-0.003, 0.044]	0.003 [-0.042, 0.049]	0.004 [-0.029, 0.036]	-0.013 [-0.058, 0.032]	0.041 [-0.102, 0.185]	0.017 [-0.019, 0.054]	0.017 [-0.023, 0.057]	-0.017 [-0.047, 0.013]
ln(BCECMP)	-0.016 [-0.042, 0.010]	-0.023 [-0.073, 0.027]	-0.015 [-0.050, 0.021]	-0.004 [-0.053, 0.046]	-0.096 [-0.254, 0.062]	0.007 [-0.033, 0.048]	-0.011 [-0.055, 0.033]	0.001 [-0.033, 0.034]
ln(BDCiPP)	0.014 [-0.013, 0.042]	0.009 [-0.043, 0.061]	-0.023 [-0.060, 0.014]	0.022 [-0.030, 0.074]	-0.030 [-0.196, 0.136]	0.006 [-0.037, 0.048]	-0.045* [-0.091, 0.001]	-0.037** [-0.072, -0.002]
ln(DPhP)	0.013 [-0.024, 0.049]	-0.003 [-0.073, 0.066]	0.025 [-0.024, 0.075]	0.034 [-0.035, 0.103]	-0.047 [-0.268, 0.173]	0.016 [-0.041, 0.072]	-0.009 [-0.070, 0.053]	0.013 [-0.034, 0.060]
ln(tb-DPhP)	-0.002 [-0.045, 0.042]	0.083* [-0.001, 0.166]	-0.060** [-0.119, -0.000]	0.011 [-0.072, 0.094]	0.188 [-0.076, 0.453]	-0.085** [-0.152, -0.017]	-0.071* [-0.144, 0.003]	-0.058** [-0.114, -0.002]
ln(o-iPr-DPhP)	0.013 [-0.032, 0.058]	-0.009 [-0.095, 0.078]	-0.020 [-0.082, 0.042]	-0.008 [-0.094, 0.078]	0.035 [-0.239, 0.310]	0.022 [-0.048, 0.092]	-0.012 [-0.088, 0.064]	-0.033 [-0.091, 0.025]
ln(Cd)	-0.007 [-0.040, 0.026]	0.006 [-0.058, 0.070]	0.005 [-0.041, 0.050]	0.003 [-0.060, 0.066]	0.049 [-0.153, 0.251]	-0.013 [-0.065, 0.039]	0.002 [-0.054, 0.058]	0.012 [-0.031, 0.055]
ln(Pb)	-0.014 [-0.057, 0.030]	-0.085** [-0.169, -0.001]	0.018 [-0.042, 0.077]	-0.012 [-0.095, 0.071]	0.051 [-0.215, 0.317]	0.072** [0.004, 0.140]	0.030 [-0.044, 0.103]	0.031 [-0.025, 0.088]
Age	-0.003*** [-0.005, -0.001]	-0.000 [-0.004, 0.004]	0.001 [-0.001, 0.004]	0.005*** [0.002, 0.009]	-0.003 [-0.016, 0.009]	-0.002 [-0.006, 0.001]	-0.004** [-0.007, -0.001]	0.004*** [0.002, 0.007]
BMI	0.000 [-0.004, 0.005]	0.003 [-0.005, 0.011]	0.002 [-0.004, 0.008]	0.004 [-0.004, 0.012]	0.005 [-0.022, 0.031]	-0.003 [-0.009, 0.004]	-0.002 [-0.009, 0.006]	0.002 [-0.003, 0.008]
Currently smoking	0.075* [-0.005, 0.155]	0.029 [-0.125, 0.182]	0.054 [-0.055, 0.164]	0.051 [-0.102, 0.203]	0.186 [-0.301, 0.674]	0.047 [-0.078, 0.171]	0.004 [-0.131, 0.139]	-0.021 [-0.124, 0.082]
Constant	1.769*** [1.433, 2.104]	0.753** [0.110, 1.396]	2.049*** [1.592, 2.506]	3.986*** [3.348, 4.623]	1.058 [-0.979, 3.096]	1.016*** [0.495, 1.537]	-1.937*** [-2.501, -1.372]	0.280 [-0.151, 0.712]
R-squared	**0.337**	**0.207**	**0.294**	**0.223**	**0.180**	**0.236**	**0.296**	**0.509**

*** p<0.01, ** p<0.05, * p<0.1

[a] Containing all non-collinear flame retardants' biological concentrations and metals with a detection percentage above 40%, and covariables age, body mass index (BMI) and smoking status, and excluding individuals with thyroid, pituitary diseases

Table S6.6. Coefficients and 95% confidence intervals in linear regression multivariable[a] models for thyroid hormones and their ratios in women (N=19)

	ln(freeT3)	ln(totalT3)	ln(freeT4)	ln(totalT4)	ln(TSH)	ln(fT3/tT3)	ln(fT4/tT4)	ln(fT4/fT3)
ln(BDE209)	-0.052** [-0.099, -0.005]	0.036 [-0.182, 0.254]	-0.001 [-0.191, 0.189]	0.031 [-0.136, 0.197]	-0.123 [-0.705, 0.458]	-0.088 [-0.267, 0.090]	-0.032 [-0.184, 0.119]	0.051 [-0.180, 0.281]
ln(BDE153)	-0.156** [-0.265, -0.047]	0.048 [-0.461, 0.556]	0.248 [-0.196, 0.691]	0.142 [-0.246, 0.530]	0.480 [-0.877, 1.838]	-0.204 [-0.620, 0.213]	0.105 [-0.248, 0.459]	0.404 [-0.134, 0.941]
ln(BDE47)	0.054* [-0.002, 0.111]	0.081 [-0.181, 0.343]	-0.130 [-0.358, 0.099]	0.031 [-0.169, 0.230]	-0.078 [-0.777, 0.621]	-0.026 [-0.241, 0.188]	-0.160* [-0.342, 0.022]	-0.184 [-0.461, 0.093]
ln(BCiPHiPP)	0.023 [-0.026, 0.071]	-0.057 [-0.282, 0.168]	0.012 [-0.184, 0.208]	0.020 [-0.152, 0.192]	-0.077 [-0.678, 0.524]	0.080 [-0.105, 0.264]	-0.008 [-0.165, 0.148]	-0.011 [-0.249, 0.227]
ln(BCECMP)	-0.032 [-0.087, 0.023]	0.077 [-0.180, 0.334]	-0.070 [-0.294, 0.153]	0.048 [-0.148, 0.244]	0.006 [-0.678, 0.691]	-0.109 [-0.319, 0.101]	-0.118 [-0.297, 0.060]	-0.038 [-0.309, 0.233]
ln(BDCiPP)	0.009 [-0.066, 0.084]	0.035 [-0.315, 0.385]	-0.214 [-0.519, 0.091]	-0.004 [-0.271, 0.263]	-0.120 [-1.054, 0.814]	-0.026 [-0.312, 0.261]	-0.210* [-0.453, 0.033]	-0.223 [-0.592, 0.147]
ln(DPhP)	0.012 [-0.069, 0.093]	-0.111 [-0.487, 0.266]	0.104 [-0.224, 0.433]	-0.110 [-0.397, 0.178]	-0.034 [-1.039, 0.971]	0.123 [-0.186, 0.431]	0.214* [-0.048, 0.475]	0.092 [-0.306, 0.490]
ln(tb-DPhP)	-0.150** [-0.249, -0.051]	0.012 [-0.449, 0.473]	-0.002 [-0.403, 0.400]	-0.021 [-0.372, 0.331]	0.329 [-0.900, 1.558]	-0.162 [-0.539, 0.215]	0.019 [-0.301, 0.339]	0.148 [-0.338, 0.635]
ln(o-iPr-DPhP)	0.018 [-0.026, 0.063]	-0.048 [-0.255, 0.159]	-0.030 [-0.211, 0.150]	-0.052 [-0.210, 0.106]	-0.063 [-0.615, 0.489]	0.066 [-0.103, 0.236]	0.022 [-0.122, 0.166]	-0.048 [-0.267, 0.170]
ln(Cd)	0.020 [-0.020, 0.061]	0.023 [-0.166, 0.212]	-0.002 [-0.167, 0.162]	0.005 [-0.140, 0.149]	0.019 [-0.485, 0.524]	-0.003 [-0.157, 0.152]	-0.007 [-0.139, 0.124]	-0.023 [-0.222, 0.177]
ln(Pb)	0.043 [-0.101, 0.187]	0.132 [-0.539, 0.803]	0.133 [-0.452, 0.719]	-0.004 [-0.516, 0.508]	0.157 [-1.634, 1.947]	-0.088 [-0.638, 0.461]	0.137 [-0.329, 0.603]	0.090 [-0.619, 0.799]
Age	-0.003* [-0.006, 0.000]	-0.003 [-0.019, 0.013]	-0.001 [-0.015, 0.013]	-0.002 [-0.014, 0.010]	-0.004 [-0.047, 0.039]	-0.000 [-0.013, 0.013]	0.001 [-0.010, 0.012]	0.002 [-0.015, 0.019]
BMI	-0.005* [-0.012, 0.001]	0.008 [-0.023, 0.039]	0.019 [-0.008, 0.046]	0.019* [-0.005, 0.042]	0.027 [-0.056, 0.109]	-0.013 [-0.039, 0.012]	0.000 [-0.021, 0.022]	0.024 [-0.008, 0.057]
Currently smoking	0.078 [-0.030, 0.187]	0.173 [-0.330, 0.677]	0.044 [-0.395, 0.483]	0.123 [-0.261, 0.507]	-0.523 [-1.867, 0.820]	-0.095 [-0.507, 0.317]	-0.079 [-0.429, 0.271]	-0.034 [-0.566, 0.497]
Constant	1.414*** [0.800, 2.028]	-0.434 [-3.295, 2.427]	1.308 [-1.186, 3.802]	3.503** [1.320, 5.686]	0.149 [-7.483, 7.782]	1.848* [-0.494, 4.190]	-2.195** [-4.183, -0.208]	-0.106 [-3.127, 2.915]
R-squared	**0.959**	**0.693**	**0.798**	**0.806**	**0.722**	**0.798**	**0.854**	**0.710**

*** p<0.01, ** p<0.05, * p<0.1

[a] Containing all non-collinear flame retardants' biological concentrations and metals with a detection percentage above 40%, and covariables age, body mass index (BMI) and smoking status, and excluding individuals with thyroid, or pituitary diseases.

Table S6.7. Coefficients and 95% confidence intervals in linear regression multivariable[a] models for reproductive hormones and their ratios in men (N=76)

	ln(FreeT)	ln(TotalT)	ln(FSH)	ln(LH)	ln(E2)[b]	ln(fT/tT)	ln(fT/E2)
ln(BDE209)	0.073 [-0.021, 0.168]	0.032 [-0.080, 0.144]	0.031 [-0.102, 0.164]	-0.004 [-0.140, 0.132]	0.066* [-0.012, 0.145]	0.042 [-0.034, 0.118]	0.004 [-0.110, 0.118]
ln(BDE153)	-0.008 [-0.149, 0.134]	-0.033 [-0.201, 0.135]	-0.164 [-0.363, 0.036]	-0.145 [-0.349, 0.059]	-0.105* [-0.228, 0.019]	0.025 [-0.089, 0.139]	0.103 [-0.068, 0.274]
ln(BDE47)	-0.018 [-0.126, 0.090]	-0.003 [-0.131, 0.125]	0.090 [-0.063, 0.242]	0.041 [-0.114, 0.197]	0.081* [-0.008, 0.170]	-0.015 [-0.103, 0.072]	-0.113* [-0.244, 0.018]
ln(BCiPHiPP)	-0.050 [-0.149, 0.049]	-0.007 [-0.125, 0.110]	-0.156** [-0.295, -0.016]	-0.073 [-0.215, 0.070]	-0.069 [-0.155, 0.017]	-0.043 [-0.123, 0.037]	0.024 [-0.096, 0.144]
ln(BCECMP)	0.033 [-0.063, 0.129]	0.093 [-0.021, 0.207]	-0.121* [-0.256, 0.015]	-0.001 [-0.139, 0.138]	0.034 [-0.044, 0.113]	-0.060 [-0.138, 0.018]	-0.004 [-0.121, 0.112]
ln(BDCiPP)	0.019 [-0.094, 0.132]	0.009 [-0.126, 0.143]	0.055 [-0.105, 0.215]	-0.056 [-0.219, 0.107]	0.001 [-0.094, 0.095]	0.011 [-0.081, 0.102]	0.026 [-0.111, 0.163]
ln(DPhP)	0.036 [-0.116, 0.188]	0.033 [-0.148, 0.214]	0.154 [-0.061, 0.369]	0.188* [-0.031, 0.408]	-0.032 [-0.159, 0.095]	0.003 [-0.120, 0.126]	0.076 [-0.109, 0.260]
ln(tb-DPhP)	-0.283*** [-0.463, -0.103]	-0.284** [-0.497, -0.070]	-0.020 [-0.274, 0.233]	-0.063 [-0.322, 0.197]	-0.074 [-0.224, 0.077]	0.000 [-0.145, 0.146]	-0.207* [-0.424, 0.010]
ln(o-iPr-DPhP)	0.057 [-0.132, 0.245]	-0.008 [-0.232, 0.216]	0.167 [-0.099, 0.433]	0.073 [-0.199, 0.345]	0.219*** [0.063, 0.375]	0.065 [-0.088, 0.217]	-0.186 [-0.414, 0.042]
ln(Cd)	-0.069 [-0.205, 0.068]	-0.025 [-0.188, 0.137]	0.119 [-0.074, 0.312]	-0.106 [-0.303, 0.091]	-0.093 [-0.207, 0.021]	-0.043 [-0.154, 0.067]	0.041 [-0.124, 0.207]
ln(Pb)	-0.012 [-0.193, 0.169]	-0.130 [-0.346, 0.085]	-0.324** [-0.580, -0.068]	0.076 [-0.186, 0.337]	0.057 [-0.097, 0.211]	0.118 [-0.028, 0.265]	-0.072 [-0.291, 0.147]
Age	-0.006 [-0.014, 0.002]	0.005 [-0.005, 0.015]	0.023*** [0.012, 0.034]	0.011* [-0.001, 0.022]	0.001 [-0.006, 0.008]	-0.011*** [-0.017, -0.004]	-0.007 [-0.016, 0.003]
BMI	-0.015* [-0.034, 0.003]	-0.044*** [-0.066, -0.023]	-0.043*** [-0.068, -0.017]	-0.032** [-0.058, -0.006]	0.007 [-0.008, 0.022]	0.029*** [0.014, 0.044]	-0.022* [-0.044, 0.000]
Currently smoking	0.022 [-0.314, 0.359]	-0.045 [-0.445, 0.355]	-0.159 [-0.634, 0.316]	0.196 [-0.289, 0.681]	0.285** [0.002, 0.568]	0.067 [-0.205, 0.339]	-0.298 [-0.705, 0.109]
Constant	5.024*** [3.620, 6.429]	2.830*** [1.161, 4.498]	3.504*** [1.521, 5.487]	1.814* [-0.212, 3.840]	4.351*** [3.175, 5.527]	2.195*** [1.058, 3.332]	0.667 [-1.033, 2.367]
R-squared	**0.298**	**0.373**	**0.488**	**0.216**	**0.318**[c]	**0.470**	**0.328**

*** p<0.01, ** p<0.05, * p<0.1

[a] Containing all non-collinear flame retardants' biological concentrations and metals with a detection percentage above 40%, and covariables age, body mass index (BMI) and smoking status, and excluding individuals with gonads, or pituitary diseases.

[b]Tobit regressions coefficients; [c]Cox-Snell pseudo-R2

Table S6.8. Coefficients and 95% confidence intervals in linear regression multivariable[a] models for reproductive hormones and their ratios in women (N=23)

	ln(Tesf)	ln(Test)	ln(Tesf/Test)
ln(BDE209)	-.072 [-.66 − .52]	-.028 [-.64 − .58]	-.044 [-.21 − .12]
ln(BDE153)	.22 [-1.5 − 1.98]	.64 [-1.2 − 2.5]	-.43* [-.92 − .067]
ln(BDE47)	-.013 [-.59 − .56]	-.054 [-.65 − .54]	.042 [-.12 − .20]
ln(BCiPHiPP)	-.036 [-.71 − .63]	-.11 [-.80 − .59]	.069 [-.12 − .26]
ln(BCECMP)	.077 [-.45 − .60]	.067 [-.48 − .61]	.011 [-.14 − .16]
ln(BDCiPP)	.10 [-.62 − .83]	-.026 [-.77 − .72]	.13 [-.072 − .33]
ln(DPhP)	-.16 [-1.0 − .68]	-.085 [-.96 − .79]	-.076 [-.31 − .16]
ln(tb-DPhP)	-.32 [-1.4 − .80]	-.091 [-1. 3 − 1. 1]	-.23 [-.55 − .082]
ln(o-iPr-DPhP)	-.18 [-.83 − .47]	-.20 [-.87 − .48]	.015 [-.17 − .20]
ln(Cd)	.23 [-.49 − .94]	.21 [-.53 − .95]	.015 [-.18 − .22]
ln(Pb)	.11 [-.27 − .50]	.11 [-.29 − .51]	-.001 [-.11 − .11]
Age	-.051** [-.097 − -.006]	-.029 [-.076 − .018]	-.022*** [-.035 − -.01]
BMI	.065 [-.021 − .151]	.048 [-.041 − .137]	.017 [-.007 − .041]
Smoking yes	.047 [-1.9 – 2.0]	-.35 [-2.3 − 1.6]	.40 [-.14 − .93]
Constant	.73 [-5.0 − 6.5]	-2.1 [-8.1 − 3.9]	2.8*** [1.2 − 4.4]
R-squared	**.74**	**.69**	**.89**

[a] Containing all non-collinear flame retardants' biological concentrations and metals with a detection percentage above 40%, and covariables age, body mass index (BMI) and smoking status, and excluding individuals with gonads, or pituitary diseases.

6.9.3. Supplementary material references

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Chapitre 7. Discussion

7.1. Discussion générale

Certains ignifuges ont été bannis ou retirés du marché à cause de leur toxicité, mais ils sont toujours présents dans l'environnement et dans les produits à recycler (Abbasi et al. 2015). La population générale y est exposée, et les travailleurs de certains secteurs industriels encore plus. Le recyclage électronique est une industrie en croissance, mais également en changement puisqu'elle suit à retardement les habitudes de consommation de la population. Il est ainsi important d'évaluer l'exposition des travailleurs du recyclage électronique à ces substances, de manière à surveiller en amont la survenue de problèmes de santé qui pourraient y être associés. L'objectif général de cette thèse était d'évaluer l'exposition à des ignifuges chez les travailleurs et d'étudier les effets endocriniens associés.

Ainsi, au cours des quatre articles scientifiques qui forment le corps de ce travail, on a tout d'abord déterminé les niveaux de base d'exposition aux PBDE dans la population générale de travailleurs canadiens. La revue systématique a ensuite compilé les niveaux d'expositions des travailleurs de différentes industries et a permis de soulever plusieurs aspects méthodologiques à considérer pour les prélèvements sur le terrain afin que les données recueillies soient fiables et reproductibles. Une étude transversale a servi à mesurer l'exposition des travailleurs du recyclage électronique à plusieurs substances, à la fois dans l'air en poste personnel et dans les fluides biologiques. Finalement, des associations avec l'équilibre endocrinien ont été explorées.

Le tableau 7.1 résume les objectifs de chaque article, ainsi que les principaux résultats. La suite du chapitre présente ensuite la contribution de cette thèse à la recherche, tout en en soulignant les aspects méthodologiques novateurs. Les considérations méthodologiques y sont également revues, de même que l'originalité de la recherche. Le chapitre se termine en présentant les perspectives et recommandations qui découlent du projet.

Tableau 7.1. Titre, objectif, et résumé des principaux résultats des quatre articles.

Article 1 (Chapitre 3) Exposure to polybrominated diphenyl ethers (PBDEs) in American and Canadian workers: Biomonitoring data from two national surveys.
Objectif : Déterminer les niveaux de polybromodiphényléthers (PBDE) dans la population active adulte américaine et canadienne avec des données d'enquêtes nationales, et identifier les industries et les professions dans lesquelles les travailleurs sont les plus exposés à certains congénères de PBDE.

Principaux résultats:
• Les congénères BDE47, -99, -100 et -153 ont été détectés dans au moins 25% des échantillons.
• Les travailleurs états-uniens ont des concentrations sériques de PBDE plus élevées que celles des travailleurs canadiens (facteur approximatif de 2 pour BDE47, 1,3 pour BDE153).
• Aux États-Unis les concentrations des travailleurs sont similaires à celles des non-travailleurs. Au Canada les concentrations des travailleurs sont environ 10-20% plus élevées que les non-travailleurs.
• Les travailleurs hommes ont des niveaux légèrement plus élevés que les travailleuses (5-10%) au Canada et aux États-Unis, avec une différence plus marquée pour le BDE153 (20-40%).
• Moyennes géométriques chez les travailleurs Canadiens :
  ○ BDE47 : 11 ng/g lipides ;
  ○ BDE99 : 3,2 ng/g lipides ;
  ○ BDE100 : 3,2 ng/g lipides ;
  ○ BDE153 : 4,4 ng/g lipides.
• Au Canada, les travailleurs des groupes Information finance, immobilier, éducation et divertissement et Commerce, transport et entreposage ont un niveau de BDE47 environ 25% plus élevé que les non-travailleurs.
• Au Canada, les travailleurs du groupe Fabrication de biens durables, et Services publics et Construction ont un niveau de BDE153 environ 50% plus élevé que les non-travailleurs

Article 2 (Chapitre 4) Assessment of occupational exposure to organic flame retardants: a systematic review.
Objectif : Compiler et porter un regard critique sur les évaluations de l'exposition professionnelle aux ignifuges dans la poussière déposée, l'air ou les fluides biologiques.

Principaux résultats :
• 58 publications ont été révisées.
• Les milieux de travail les plus étudiés sont les édifices de bureaux (16 études) et le recyclage électronique (15 études).
• Les concentrations moyennes dans l'air les plus élevées de BDE209 et le TPhP ont été mesurées dans l'industrie du recyclage électronique (2170 ng/m³ et 850 ng/m³, respectivement).
• La concentration moyenne sanguine la plus élevée de BDE209 a été mesurée chez des travailleurs d'un fabricant de câbles électriques (52 ng/g lipides).
• Plusieurs lacunes méthodologiques soulevées, dont :
  ○ peu de recherches sur les ignifuges de substitution (NBFR, OPE) ;
  ○ méthodes de prélèvement d'air ou de poussières peu reproductibles ;
  ○ manque d'études sur les corrélations entre les différents médias et sur les professions particulièrement concernées ;
  ○ méthodes statistiques pas toujours adéquates pour les jeux de données avec une forte proportion sous la limite de détection (censurées à gauche).

Article 3 (Chapitre 5) Halogenated flame retardants and organophosphate esters in the air of electronic waste recycling facilities: Evidence of high concentrations and multiple exposures.
Objectif : Évaluer l'exposition des travailleurs du recyclage électronique au Québec à 40 ignifuges dans l'air, et identifier les principaux cofacteurs d'exposition.
Principaux résultats : • 39 ignifuges détectés dans le recyclage électronique; 26 dans le recyclage commercial. • Les concentrations dans l'air de tous les ignifuges sont de deux à 500 fois plus élevées dans le recyclage électronique que dans le recyclage commercial. • Parmi les quatre groupes chimiques d'ignifuges, les PBDE représentent de 14 à 82% de l'exposition dans le recyclage électronique, et les OPE représentent 98% de l'exposition dans le recyclage commercial. • Une augmentation de trois ans d'ancienneté est associée à une exposition à tous les ignifuges plus faible d'environ 15%. • Les tâches de démantèlement et de compactage sont associées à des expositions d'ignifuges (sauf pour le Allyl 2,4,6-tribromophenyl ether) en moyenne 2,2 et 1,4 fois plus élevées que celle de supervision, respectivement. • La manipulation de téléviseurs CRT ou LCD/LED/Plasma, est associée à des concentrations d'ignifuges en moyenne 3,3 et 2,5 fois plus élevées que la non-manipulation de matériel.
Article 4 (Chapitre 6) Multi-exposures to endocrine disruptors in electronic waste recycling workers: associations with thyroid and reproductive hormones.
Objectif : Mesurer les concentrations biologiques de PBDE et de OPE et évaluer leur association avec les niveaux d'hormones thyroïdiennes et sexuelles.

Principaux résultats :
• Les moyennes géométriques des ignifuges mesurés sont plus élevées de 10 à 1000% dans le recyclage électronique que dans le recyclage commercial, sauf pour les BDE47 et BDE153.
• Moyennes géométriques du PBDE et de l'OPE les plus élevée dans le recyclage électronique :
  ○ BDE209: 18 ng/g lipides (environ neuf fois la concentration dans le groupe de recyclage commercial ou la population générale de travailleurs);
  ○ DPhP et BClPHiPP : 1,7 ng/ml (environ deux fois la concentration dans le recyclage commercial pour le DPhP et 1,5 fois plus pour le BClPHiPP).
• L'ACP montre que le BDE209 et le plomb ont tendance à être retrouvés à forte concentration concurremment chez les travailleurs du recyclage électronique.
• Pas de tendances notables dans les associations mesurées entre les concentrations d'ignifuges et celles des hormones thyroïdiennes.
• Tendance générale à des associations négatives entre des métabolites d'OPE et la testostérone, et positives avec l'estradiol chez les hommes.
• Quelques associations ponctuelles observées entre les concentrations de PBDE et les métabolites d'OPE et les ratios d'hormones thyroïdiennes, sans qu'une tendance générale se dégage.
• Les fluctuations observées ne représentent pas des variations hormonales pathologiques.

7.2. Contributions de la recherche

7.2.1. Exposition aux ignifuges

Exposition de base des travailleurs de la population générale (Article 1)

La stratégie de diagnostic de l'exposition professionnelle requiert d'une part des mesures de l'exposition, et d'autre part, une valeur de référence à laquelle on peut comparer cette exposition (Mulhausen et al. 2015). Or, il n'existe pas de valeur limite d'exposition en milieu de travail pour les ignifuges, sauf pour le TPhP dont la valeur a été établie pour prévenir de la neurotoxicité, ainsi que l'irritation oculaire et cutanée. La comparaison des valeurs d'exposition professionnelle aux valeurs dans la population générale peut renseigner sur la contribution additionnelle à l'exposition représentée par le milieu de travail. Afin de situer les concentrations mesurées en milieu de travail par rapport à la population générale active, deux bases de données d'enquête populationnelles pertinentes sont disponibles. Ces enquêtes cycliques, effectuées sur un échantillon représentatif de la population nationale, sélectionnent aléatoirement des sous-groupes de participants chez qui différentes substances chimiques sont mesurées dans les fluides biologiques. Les concentrations des substances mesurées sont présentées dans des rapports statistiques, mais sont regroupées par strate d'âge et par sexe, sans égard au statut de travail. De plus, grâce aux données d'emploi des participants à ces enquêtes, il est possible de déterminer s'il existe des différences d'exposition entre les non-travailleurs et les travailleurs de différentes industries. Il est en effet reconnu que les expositions à certains ignifuges à domicile soient considérables, et que le statut socioéconomique (et conséquemment, le type d'emploi) soit également un facteur important (Kalantzi and Pagoni 2019), ce qui pourrait expliquer une signature d'ignifuges différente entre les travailleurs et les non-travailleurs.

Ainsi, l'article 1 (Chapitre 3) a fourni des valeurs de base pour l'exposition aux PBDE (Tableau 3.3), les seuls groupes chimiques d'ignifuges pour lesquels il existait des données populationnelles nord-américaines au moment de sa publication. L'exposition biologique aux PBDE de Canadiens et d'États-Uniens, est présentée dans la même étude. L'article 1 présente également une manière d'exploiter les données d'emploi et d'industries en regroupant les données selon les expositions professionnelles potentielles aux ignifuges.

Des différences d'exposition considérables entre le Canada et les États-Unis ont été mises en évidence, ce qui avait auparavant été rapporté de manière anecdotique (Kim et al. 2018), mais jamais au sein de la même analyse et avec une telle taille d'échantillon. Dans les deux bases de données, les concentrations sanguines du congénère BDE153 sont particulièrement plus élevées chez les hommes travailleurs que chez les femmes dans les deux bases de données, ce qui a été rapporté à quelques reprises pour ce congénère particulier (Bjermo et al. 2017; Toms et al. 2018). Les moyennes géométriques chez les travailleurs canadiens étaient de 11 ng/g lipides pour le BDE 47, et de 4.4 ng/g lipides pour le BDE153. De plus, il n'y avait pas ou peu de différences d'exposition, dans les deux bases de données, entre les non-travailleurs et les travailleurs des différentes industries pour les PBDE faiblement bromés (comme le BDE47, BDE99 ou BDE100), mais des différences sont observées pour le BDE153 au Canada. Par exemple, les travailleurs des groupes Fabrication de biens durables et Services publics et construction avaient des concentrations de BDE153 environ 50% plus élevées que celles des non-travailleurs.

Expositions dans des milieux de travail plus propices à la présence d'ignifuges (article 2)

Nous avons vu qu'il y a une exposition de base aux ignifuges dans la population générale, et que cette exposition peut être encore plus élevée chez les travailleurs, et ce, particulièrement dans certains secteurs d'activité. Cependant, les catégories d'industries manquent de précision pour identifier les milieux spécifiques où les expositions sont plus importantes. La connaissance des niveaux d'exposition recensés dans les milieux de travail et chez les travailleurs permet de situer un milieu de travail d'intérêt par rapport à d'autres contextes professionnels et d'orienter les efforts de prévention. De plus, puisque plusieurs méthodes différentes sont utilisées pour prélever et analyser les ignifuges, une compilation et un regard critique sur ces méthodes permettent de juger de la qualité et de la comparabilité des études. Cela offre également l'opportunité d'émettre des recommandations sur les méthodes de prélèvement à privilégier.

L’article 2 (Chapitre 4) consiste en une revue systématique qui a recensé les niveaux d’ignifuges mesurés dans 58 publications, tous milieux de travail confondus, afin de brosser un portrait des milieux ou professions qui mériteraient plus d’attention de la part des chercheurs et des hygiénistes du travail. On y présente une compilation inédite des concentrations d’ignifuges dans plusieurs milieux de travail, avec différents médias d’échantillonnage et pour quatre groupes chimiques d’ignifuges. Les méthodes d’échantillonnage de l’air, des poussières déposées, ainsi que des liquides biologiques ont été compilées et critiquées. Les limites des articles publiés sur l’exposition professionnelle aux ignifuges ont été identifiées et des recommandations ont été émises en conséquence.

On y a ainsi constaté que le recyclage électronique était parmi les milieux de travail où se retrouvaient les plus hautes concentrations en PBDE et en OPE dans l’air et les poussières déposées et qu’il n’y avait pratiquement aucune donnée nord-américaine à ce sujet. Les données biologiques de PBDE révélaient que les recycleurs de mousse de polyuréthane présentaient des concentrations sanguines de BDE47 cinquante fois plus élevées que les travailleurs de la population générale canadienne, ce qui concorde avec la présence connue de ce congénère dans ce type de produit (Stapleton et al. 2012). A contrario, les écoles et garderies présentaient des niveaux d’ignifuges généralement plus bas que les autres milieux de travail. L’article 2 a identifié plusieurs problèmes et a proposé des améliorations méthodologiques et des pistes de recherche qui visent à améliorer d’une part la collecte et l’analyse des données, et d’autre part les connaissances au sujet de l’exposition professionnelle aux ignifuges. En particulier, il y avait peu de données d’exposition sur les ignifuges de substitution utilisés plus récemment, comme les OPE et les NBFR. Certains milieux de travail présentaient des niveaux particulièrement élevés d’ignifuges, comme celui du recyclage électronique, mais aussi les avions et les automobiles. Les travailleurs dans la fabrication de câbles et les pompiers présentent également des concentrations biologiques assez élevées de PBDE. Les méthodes de prélèvement sont cependant très diverses et leur reproductibilité est difficile à assurer, principalement en ce qui a trait au prélèvement des poussières déposées. Finalement, les méthodes statistiques employées pour analyser les données sont souvent très peu détaillées et présentent des lacunes, comme l’omission de présenter le pourcentage de valeurs non détectées ou le traitement statistique de ces valeurs, l'application de méthodes qui requièrent la normalité sur un jeu de données lognormal non transformé, ou même l'omission complète de description des méthodes statistiques employées.

Exposition des travailleurs du recyclage électronique (Articles 3 et 4)

Le recyclage électronique constitue un milieu de travail propice à des expositions élevées aux ignifuges. De plus, il s'agit d'une industrie en pleine croissance dans le contexte d'un intérêt grandissant pour l'économie circulaire et les emplois verts. Toutefois, aucune documentation de ce secteur d'activité n'avait été publiée au Canada au moment du début du projet de recherche. Le milieu du recyclage électronique connaît un fort taux de roulement de personnel, le matériel qui y est traité change au gré des arrivages, et les méthodes de travail varient selon l'entreprise. Ces facteurs ont justifié l'utilisation d'un devis transversal dans cette industrie, afin d'obtenir un instantané d'une situation très variable.

À la lumière des informations recueillies et analysées dans l'article 2, plusieurs aspects ont été considérés pour la stratégie d'échantillonnage du projet IRSST. En effet, l'importance du milieu collecteur pour les ignifuges a été soulignée et a justifié l'utilisation de tubes OVS qui permettent à la fois de prélever les formes particulaires et gazeuses des substances ignifuges. De plus, considérant la grande variabilité des méthodes de collecte des poussières déposées et le manque de comparabilité entre les études, il a été choisi de ne pas utiliser ce médium. La mesure des ignifuges dans l'air a permis une estimation de l'exposition potentielle, et la mesure dans les liquides biologiques a estimé la charge corporelle, ce qui est préférable pour mesurer les associations avec les hormones (voir la section suivante). Nous avons également tenté d'identifier des déterminants de l'exposition aux ignifuges comme les tâches ou le matériel manipulé, puisque ces renseignements n'étaient pas rapportés dans la littérature et pourraient permettre de cibler les interventions en hygiène du travail. Cet aspect de l'étude a toutefois constitué un défi de taille en pratique, dû à la difficulté de suivre plusieurs travailleurs qui pouvaient changer de tâche durant la journée, avec un nombre limité d'hygiénistes sur le terrain. Les aspects de l'analyse statistique des données et de la présentation des résultats ont également exigé une réflexion particulière afin d'exploiter les données de manière optimale. Un certain pourcentage de données situées sous la limite de détection est attendu dans le cadre d'une campagne de prélèvement de l'air ou de marqueurs biologiques. L'article 3 a présenté des approches pour utiliser les données non détectées autrement que par une substitution simple, qui est la méthode la plus fréquemment utilisée, mais également la plus susceptible aux biais (Hewett and Ganser 2007; Huynh et al. 2014).

Les travailleurs du recyclage électronique de notre étude étaient exposés à des concentrations d'ignifuges relativement élevées comparativement au groupe du recyclage commercial et aux autres milieux de travail décrits dans la littérature. En ce qui concerne les PBDE, la concentration moyenne géométrique de BDE209 dans l'air mesurée dans l'entreprise de grande taille, soit 5100 ng/m³, est plus de deux fois supérieure au maximum le plus élevé rapporté dans la littérature, dans un avion (Allen et al. 2013a). Toutefois, les concentrations des autres congénères de PBDE mesurés, quoique plus élevées que dans le recyclage commercial, ne sont pas très élevées par rapport à d'autres milieux de travail ou à des milieux résidentiels. Dans des maisons canadiennes, une concentration moyenne de 0,25 ng/m³ de BDE47 avait été mesurée (Okeme et al. 2018) alors que la moyenne la plus élevée dans le recyclage électronique était de 2,8 ng/m³. Ceci indique que la présence importante de BDE209 pourrait être caractéristique du recyclage électronique, mais pas nécessairement les autres congénères des PBDE. En ce qui a trait aux OPE, les concentrations mesurées les plus élevées sont de quatre à cent fois plus élevées que les mesures domestiques dans une étude canadienne (Okeme et al. 2018), et de 6 à 15 inférieures aux données domestiques d'une autre étude canadienne (Yang et al. 2019). Les données d'exposition aux OPE dans d'autres études sur le recyclage électronique font également état de concentrations beaucoup plus élevées que ce que nous avons mesuré. Cela nous porte à croire que l'exposition aux OPE est très variable et ne serait pas tout à fait un indicateur spécifique de l'exposition dans le recyclage électronique, contrairement au BDE209.

La plupart des tâches exposaient les travailleurs du recyclage électronique à des concentrations plus élevées de PBDE, d'ignifuges chlorés et d'OPE que la tâche de superviseur. De plus, nous avons observé des concentrations plus élevées dans une entreprise de grande taille comparativement aux petites entreprises, ce qui concorde avec d'autres observations sur les expositions aux métaux dans le recyclage électronique états-unien (Ceballos et al. 2017).

Les données d'exposition aux ignifuges par le biais d'indicateurs biologiques sont présentées dans l'article 4 (chapitre 6). Nous constatons que les travailleurs du recyclage électronique, de même que les travailleurs du recyclage domestique, ont des niveaux d'exposition au BDE47 plus bas, environ de moitié, que les travailleurs canadiens. Il est possible que cela soit dû au fait que les données canadiennes aient été colligées il y a plus de 10 ans, et que le mélange commercial contenant le BDE47 (pentaBDE) ait vu son utilisation diminuer au cours des dernières années. En effet, certains auteurs ont observé une tendance à la baisse des niveaux sanguins de BDE47 dans la population nord-américaine (Cowell et al. 2019). Toutefois, la moyenne géométrique de BDE209 dans le recyclage électronique de 18 ng/g lipides est dix fois plus élevée que dans le groupe de recyclage commercial et dans la population générale canadienne (Tableau 1.1). Le BDE209 sanguin est donc probablement associé à une exposition professionnelle plus importante qu'à une exposition environnementale, et semble caractéristique du recyclage électronique au même titre que l'exposition correspondante dans l'air. Toutefois, les données colligées dans l'article 2 (Tableau 4.2) montrent des concentrations de BDE209 sanguin allant jusqu'à 268 ng/g lipides dans la fabrication de câbles, ce qui ferait du recyclage électronique un milieu exposé, mais probablement pas le plus important. En ce qui a trait aux OPE, les concentrations de métabolites urinaires mesurées dans le recyclage électronique sont légèrement supérieures à celles du groupe de recyclage commercial, mais elles sont similaires ou inférieures à des données rapportées dans la population générale (Tableau 1.2) ou dans d'autres milieux de travail (Tableau 4.2). Les métabolites urinaires d'OPE, tels que nous les avons mesurés, ne sont donc probablement pas un bon indicateur de l'exposition professionnelle à ces ignifuges, et ne constitueraient pas une des expositions principales dans le recyclage électronique, à l'instar des mesures dans l'air de ces ignifuges.

Signature de l'exposition des travailleurs (articles 3 et 4)

En plus de connaître les niveaux d'exposition, il est intéressant d'illustrer l'exposition à plusieurs substances en fonction de certaines variables. En effet, cela peut renseigner sur l'existence d'une « signature » de contaminants dans l'environnement ou dans un milieu de travail spécifique. Cela permet d'apprécier la contribution relative de chaque contaminant à l'exposition totale, ou encore d'identifier la source des expositions.

Les profils d'exposition dans l'air des travailleurs ont été illustrés dans l'article 3 par le biais d'un diagramme à bandes (figure 5.1) qui permet d'apprécier les expositions en termes de concentrations relatives, et révèle ainsi les différences proportionnelles entre les expositions des différents groupes. Enfin, une illustration des profils d'exposition biologiques aux contaminants des travailleurs du recyclage, comparativement au recyclage commercial, a été effectuée par le biais d'une analyse en composantes principales dans l'article 4 (figure 6.1).

La signature d'ignifuges diffère entre les entreprises de recyclage électronique de différentes tailles, et entre le secteur du recyclage électronique et celui du recyclage domestique. En effet, plus la taille de l'entreprise augmente, plus la proportion relative des OPE diminue en faveur de celle des PBDE. Cela témoigne probablement d'un plus grand volume de traitement d'articles électroniques plus âgés, contenant le mélange commercial décaBDE (Abbasi et al. 2016). Grâce à la représentation graphique des deux premières composantes de l'ACP, les expositions concurrentes les plus communes pour chacun des deux groupes observés (recyclage électronique et recyclage commercial) sont mises en évidence. Il y apparaît évident que les différences principales entre les deux groupes résident dans la co-exposition élevée au plomb et au BDE209 chez les travailleurs du recyclage électronique, alors que les groupements d'expositions aux OPE semblent similaires entre les deux secteurs d'activité. L'exposition aux OPE semble donc avoir une source majoritairement environnementale ou domestique plutôt que professionnelle.

7.2.2. Effets endocriniens (Article 4)

Les données *in vitro*, animales et épidémiologiques montrent que les ignifuges sont des substances qui peuvent perturber l'équilibre endocrinien. Cependant, tel que mentionné précédemment, les éléments de preuve ne sont pas encore suffisants et cohérents, principalement au niveau des effets chez l'humain dans les études épidémiologiques. Dans la perspective où la perturbation endocrinienne est un mécanisme d'action pouvant éventuellement entraîner un problème de santé, la mise en évidence d'une association entre l'exposition à des ignifuges et les niveaux hormonaux pourrait représenter une indication précoce de l'apparition de tels problèmes. Toutefois, la mise sur pied d'études épidémiologiques de grande taille est un défi, notamment à cause du coût des analyses de laboratoire, et un nombre minimal de participants doit être atteint pour obtenir une puissance statistique suffisante pour déceler des effets. Nous avions calculé lors de la préparation du protocole qu'une taille d'échantillon de 100 personnes (50 exposés et 50 non-exposés) permettrait de mettre en évidence une différence minimale détectable d'environ la moitié de l'écart-type avec une puissance de 80%. Ces calculs avaient été possibles pour l'estradiol, la testostérone, T4 total et TSH, pour lesquels on aurait pu détecter une différence minimale de 0,47 pg/L, 0,15 ng/L, 14 nmol/L et 0,51 mIU/L, respectivement. Une revue non systématique de la littérature (Tableau S 6.1) a permis d'affirmer que 11 des 24 études sur les effets endocriniens des ignifuges chez les adultes ont des tailles d'échantillon inférieures à 100 participants et n'auraient probablement pas été suffisamment puissantes pour déceler de petites différences de concentrations hormonales.

Notre étude a mesuré chez cent travailleurs les niveaux d'hormones thyroïdiennes, mais également les hormones sexuelles, lesquelles sont plus rarement étudiées en relation avec l'exposition humaine aux ignifuges. De plus, nous avons étudié les associations avec les ratios d'hormones, soit le rapport entre les phases libres et conjuguées pour les hormones thyroïdiennes, et le rapport entre une hormone et son précurseur pour les hormones thyroïdiennes et sexuelles. Les variations des ratios d'hormones peuvent révéler des informations sur la capacité de l'organisme à s'adapter aux perturbations physiologiques, ainsi que sur les mécanismes d'action potentiels d'un perturbateur externe, par exemple par un effet sur les protéines de transport ou sur les enzymes métaboliques (Sollberger and Ehlert 2016). L'analyse en composantes principales nous a permis d'identifier des composantes dont l'effet combiné a ensuite été exploré à l'aide de régressions pour mettre en évidence des associations entre des expositions concomitantes aux ignifuges et les niveaux d'hormones.

Des associations significatives ont été observées entre l'exposition aux ignifuges des deux groupes chimiques pour lesquels des biomarqueurs étaient disponibles et les concentrations d'hormones thyroïdiennes et sexuelles. Une association positive a en effet été observée chez les hommes entre le BDE209 et l'hormone T4 totale, ainsi qu'une association négative entre le métabolite tb-DPhP et l'hormone T4 libre. Chez les femmes, des associations négatives ont été observées entre l'hormone T3 libre et le BDE153, de même qu'avec le tb-DPhP. La présence d'associations, ou encore le sens des associations observées entre les ignifuges et les hormones thyroïdiennes ne concordent cependant pas avec les résultats d'études similaires déjà publiées, quoique celles-ci aient déjà peu de similitudes entre elles. Il est possible les variations intra- et interindividuelles soient trop grandes pour les associations observées avec notre taille d'échantillon ou encore qu'un devis transversal soit sous-optimal pour mettre en évidence les perturbations endocriniennes. En ce qui a trait aux hormones sexuelles, des associations négatives ont été observées chez l'homme entre le tb-DPhP et la testostérone libre et la testostérone totale (diminution de 18% et 19% pour une augmentation du double de la concentration du métabolite, respectivement). Un autre métabolite d'OPE, le o-iPr-DPhP, était associé à une augmentation de 21% de l'hormone estradiol chez l'homme. Une seule étude semble avoir exploré les associations entre les hormones sexuelles et les métabolites d'OPE chez les hommes (Meeker et al. 2013a); cette étude comprenait seulement 33 hommes issus d'une clinique de fertilité, chez qui aucune association n'a été identifiée avec la testostérone ou l'estradiol. Considérant la force de l'association que nous avons mesurée, nos résultats suggèrent toutefois que les métabolites d'OPE pourraient être associés aux hormones sexuelles chez les hommes. De plus, le ratio de la testostérone sur l'estradiol était diminué de 15% en association avec un doublement de la concentration en tb-DPhP urinaire, ce qui pourrait suggérer une action stimulante sur les aromatases responsables du métabolisme de la testostérone en estradiol (Norris and Carr 2013). Cela a déjà été observé avec d'autres polluants comme l'atrazine dans des modèles cellulaires, quoiqu'il ne s'agisse pas d'une molécule organophosphorée (De Coster and van Larebeke 2012). Enfin, les associations observées entre certains ignifuges et des hormones ou leurs ratios suggèrent des perturbations qui peuvent résider au niveau sub-clinique et ne correspondent pas nécessairement à des variations pathologiques. Les résultats méritent tout de même une attention quant à leurs conséquences éventuelles sur la santé reproductive ou métabolique.

7.3. Considérations méthodologiques

Chaque article contenu dans cette thèse énumère les considérations méthodologiques qui lui sont propres. Cependant, certains points méritent d'être soulignés par rapport à l'ensemble du projet de recherche.

Tout d'abord, dans le cadre du premier article, il n'était pas possible d'identifier spécifiquement un seul groupe d'industrie présenté dans l'article 1 qui comprendrait l'ensemble des travailleurs du recyclage électronique. En effet, ce type de recyclage peut être classé dans différents groupes industriels selon leur vocation principale, comme Commerce de détail pour les entreprises ayant des activités de réemploi, ou encore au secteur Services professionnels, scientifiques et techniques pour les entreprises offrant des activités d'effacement de données. Cela rend difficile la comparaison plus précise entre les valeurs d'exposition aux PBDE des travailleurs du recyclage électronique et celles d'un autre groupe industriel. D'ailleurs, la faible taille d'échantillon dans certains groupes industriels nous a contraints à les rassembler, ce qui limite le niveau de détail. De plus, des valeurs biologiques individuelles pour les ignifuges bromés n'étaient disponibles que pour un seul cycle de l'ECMS et de NHANES (les échantillons biologiques ayant été regroupés dans les cycles d'étude suivants), et aucun cycle de ces études ne contenait de mesures urinaires pour les OPE au moment de la préparation des articles de cette thèse. Cela limite la taille d'échantillon disponible, et explique l'âge des données.

Le devis utilisé pour la collecte de données des articles 3 et 4 (chapitres 5 et 6) est de nature transversale et comporte les limites associées à ce genre de devis quant à l'interprétation des résultats. Il s'agit un instantané de la situation dans le recyclage électronique tant au niveau des expositions que des associations avec les hormones mesurées. En ce qui a trait aux expositions, la nature extrêmement variable des déchets électroniques traités, même à l'intérieur d'une même semaine de travail, en plus du devis transversal font que les résultats et conclusions qui sont tirés ne peuvent pas être extrapolés directement à l'ensemble du secteur d'activité au Canada ni aux expositions subies par les travailleurs tous les jours. De plus, bien que nous ayons tenté de minimiser l'interférence entre notre présence et les activités habituelles des entreprises participantes, il est impossible d'exclure la possibilité que les travailleurs aient modifié leurs méthodes de travail ou leurs habitudes sanitaires lors de notre visite. En ce qui concerne les mesures d'association, il est impossible d'en estimer la temporalité puisque les variables dépendantes et indépendantes ont été mesurées en même temps.

La nature transversale de notre projet a également imposé des choix méthodologiques visant à optimiser la participation des entreprises et des sujets. C'est pourquoi nous avons dû procéder aux prélèvements sur deux jours consécutifs, l'un pour prélever les ignifuges, et l'autre pour prélever les métaux. Ceci demandait donc deux jours de participation de la part des travailleurs, mais permettait d'éviter le port de deux pompes pendant une même journée, ce qui aurait été difficile pour certains travailleurs. Cela nous a aussi permis de récolter deux échantillons d'urine distincts plutôt que d'en séparer un seul pour les différentes analyses, ce qui simplifie les manipulations au laboratoire. De plus, il aurait été préférable de prélever le sang à la fin de la semaine (vendredi) pour refléter le plus possible l'exposition des substances avec une demi-vie plus longue comme les PBDE ou le plomb. Cependant, l'obligation de gérer les échantillons au laboratoire le soir même ou le lendemain matin nous a contraints à effectuer ces prélèvements le jeudi. De plus, nous avons été confrontés à des abandons de la part de participants, ce qui explique que nous ayons 103 échantillons d'air pour les ignifuges et pour les métabolites urinaires d'OPE, ainsi que 100 pour les mesures de PBDE dans le plasma et 101 pour les données sociodémographiques.

Par ailleurs, les indicateurs biologiques mesurés ont des demi-vies variables d'une substance à l'autre et qui ne sont pas bien connues chez l'humain en ce qui a trait aux ignifuges ; ainsi, il n'est pas certain que l'exposition mesurée dans les liquides biologiques à la fin d'un quart de travail reflète réellement l'exposition dans l'air de la même journée. Il n'a pas été possible de mesurer tous les métabolites de chaque substance mère, ce qui ne permet pas une estimation précise de la charge corporelle. C'est le cas par exemple du TDCiPP pour lequel seulement deux des quatre métabolites connus ont été mesurés, ou encore pour le TCEP dont un des métabolites majeurs, le bis (2-chloroéthyl) phosphate (Van den Eede et al. 2013), n'était pas mesurable par le laboratoire d'analyse consulté, faute de méthode analytique validée. La mesure des ignifuges et de leurs métabolites, dans l'air ou dans les liquides biologiques, est une expertise en développement, ce qui restreint l'éventail des analyses chimiques possibles par ses aspects techniques, mais également par les coûts élevés associés.

Des facteurs non mesurés ont pu influencer les niveaux hormonaux rapportés dans l'article 4 (chapitre 6). Notamment, les travailleurs du e-recyclage sont exposés à de nombreuses substances considérées comme perturbateurs endocriniens que nous n'avons pas mesurées dans les liquides biologiques, comme les déchloranes, les nouveaux ignifuges bromés, le bisphénol A, le tetrabromobisphenol-A et d'autres plastifiants (Bakhiyi et al. 2018; Gore et al. 2015). En plus des facteurs énoncés dans l'article 4, les variabilités interindividuelles et intra-individuelles des niveaux hormonaux sont difficiles à prendre en compte dans le devis utilisé et avec un échantillon de 100 individus. Par exemple, la variation circadienne de l'hormone TSH peut atteindre 50% (Fisher 1996), ce qui est bien au-delà des effets que nous avons mesurés. Les autres hormones thyroïdiennes ont par contre des niveaux plutôt stables chez un même individu, mais l'étendue des valeurs normales dans une population est large (Koulouri et al. 2013). De même, les étendues normales pour les hormones sexuelles sont assez larges, indiquant une variabilité interindividuelle notable. Le Tableau 6.3 présente les valeurs considérées normales par le laboratoire ayant effectué les analyses.

Finalement, les nombreuses analyses réalisées dans les articles posent la difficulté inhérente aux comparaisons multiples. Chaque test statistique en soi présente la possibilité qu'une association significative ne soit en fait due qu'à la chance. Lorsque le nombre de tests augmente, on peut calculer la probabilité qu'au moins l'un d'entre eux soit significatif. Par exemple, dans l'article 4, le calcul $1\text{-}(1\text{-}\alpha)^n$ (Rothman 1990), où α est généralement fixé à 5% et dans notre cas $n = 364$ pour chaque association entre une covariable et une hormone révèle une probabilité de 100% d'observer au moins une association significative qui serait due à la chance. En considérant 364 intervalles de confiance à 95% calculés pour chacune des hormones, nous pouvions nous attendre à ~18 associations significatives dues à la chance. Nous en avons observé 42 (Tableaux S 6.5 à S 6.8) qui de surcroît présentaient des tendances systématiques peu compatibles avec le hasard (sens des associations chez les hommes et les femmes, associations avec les hormones sexuelles), ce qui suggère que plusieurs d'entre elles reflètent plausiblement une association réelle.

7.4. Originalité de la recherche

Les travaux effectués dans le cadre de cette thèse font preuve d'originalité à plusieurs égards. Tout d'abord, l'analyse conjointe des deux bases de données populationnelles permet d'employer la même méthodologie d'analyse, ce qui augmente la comparabilité des données. De plus, le contexte socio-économique de ces deux pays est semblable, ce qui accroît l'échantillon et a le potentiel de consolider les conclusions. Au-delà des comparaisons entre les pays, l'exploitation des variables relatives à l'emploi des participants de ces bases de données est très rare, et n'avait même jamais été effectuée pour les données canadiennes, bien que ces bases de données représentatives de la population générale soient riches en variables dont certains aspects sont sous-exploités (Bain et al. 1997; Sobus et al. 2015).

Ensuite, l'article 2 consiste en la première revue de littérature à rapporter de manière systématique l'exposition professionnelle aux ignifuges. De plus, il s'agit à notre connaissance de la première revue de données d'exposition professionnelle ayant suivi le guide PRISMA de manière rigoureuse pour rapporter de manière transparente sa méthodologie et ses résultats. Finalement, bien que les défis expérimentaux de l'analyse de laboratoire des ignifuges aient déjà été soulevés (Covaci et al. 2011; Fulara and Czaplicka 2012), les problèmes méthodologiques relatifs au prélèvement des échantillons et à l'analyse statistique des données de mesure n'avaient jamais été énoncés jusqu'à présent.

Ces éléments précurseurs ont encadré la recherche effectuée sur le terrain, tout en fournissant des données utiles à l'interprétation des résultats. En effet, cette recherche est la première en Amérique du Nord à évaluer simultanément l'exposition de travailleurs du recyclage électronique par le biais de mesures dans l'air en poste personnel et d'indicateurs biologiques. D'ailleurs, des analyses sont en cours pour évaluer l'association entre les deux médias. Plus de 40 ignifuges ont été mesurés dans l'air, 13 dans des échantillons de sang et 15 en tant que métabolites urinaires auprès d'une centaine de travailleurs, faisant de cette étude la plus ambitieuse réalisée dans ce milieu de travail. Cette recherche a aussi mis en évidence une « signature » du mélange d'ignifuges les plus souvent retrouvés dans ce secteur d'activité et en fonction de la taille de l'entreprise. Ces résultats, qui n'avaient pas été rapportés auparavant, sont directement transposables en milieu de travail car ils peuvent servir aux intervenants de santé publique à cibler les substances à mesurer en entreprise. De plus, une méthode statistique semi-paramétrique (régression de Cox inversée) a été employée afin de consolider les conclusions générales obtenues à partir des analyses Tobit, pour identifier les tâches ou intrants les plus exposants.

Finalement, l'étude de la perturbation endocrinienne dans un contexte de santé au travail a une visée préventive plutôt que diagnostique, puisqu'il ne s'agit pas d'un effet associé à une normalité des valeurs cliniques ou à une pathologie franche. La perturbation des hormones thyroïdiennes et sexuelles a été explorée sous des angles novateurs ou peu communs, tels que par l'utilisation des ratios d'hormones, de régressions sur composantes principales, et par la mesure de substances provenant de différents groupes chimiques. Il s'agit notamment de la première étude à montrer des associations entre des métabolites d'OPE et les hormones sexuelles chez des adultes, et de la première étude des associations entre les ignifuges et les hormones dans le recyclage électronique en Amérique du Nord.

7.5. Perspectives et recommandations

Cette étude a mis en évidence que certaines expositions aux ignifuges dans l'industrie du recyclage électronique au Québec étaient plus élevées que dans la population générale et dans d'autres secteurs industriels. Elle a également montré une association entre l'exposition à certains de ces ignifuges et les niveaux d'hormones thyroïdiennes et sexuelles. Ces informations peuvent orienter de futures actions en santé au travail et guider les recherches dans des domaines sous-développés.

Les données d'enquêtes populationnelles utilisées dans l'article 1 sont riches et permettent de connaître les niveaux de base à plusieurs contaminants. Il est regrettable que les ignifuges ne soient pas systématiquement mesurés à tous les cycles des deux enquêtes consultées. Cependant, des données d'ignifuges OPE sont disponibles pour l'enquête NHANES depuis 2017 pour le cycle 2013-2014. Il serait intéressant de procéder à une analyse similaire pour obtenir des données comparables aux données rapportées dans les milieux de travail. De plus, les différences que nous avons observées entre les non-travailleurs et les travailleurs de certaines industries pourraient être explorées en regard d'autres contaminants, comme des métaux (résumé présenté par l'étudiante au congrès EPICOH en 2017) ou d'autres substances organiques suspectées d'avoir une source professionnelle importante.

Selon les données colligées dans l'article 2, l'industrie du recyclage électronique, ainsi que d'autres milieux de travail comme celui de la fabrication de câbles ou encore le métier de pompier mériteraient une surveillance particulière des hygiénistes et des chercheurs, surtout dans les entreprises de grande taille. Dans un objectif d'évitement prudent, ces entreprises gagneraient à diminuer les expositions le plus possible afin de prévenir l'apparition potentielle de problèmes de santé relatifs à la perturbation endocrinienne. Bien qu'il n'existe pas de valeur limite d'exposition professionnelle aux ignifuges, nous avons vu que le BDE209 pouvait servir de marqueur de l'exposition dans le recyclage électronique, puisqu'il s'agit de la substance la plus prévalente dans l'air de ces entreprises et dans le sang des travailleurs. La recherche n'avait pas pour but d'identifier des moyens de maîtrise de l'exposition (ventilation, port de gants, port du masque, lavage des mains …) particulièrement efficaces pour réduire l'exposition. Cependant la gestion et le port d'équipement de protection personnelle (ÉPI) n'étaient pas optimaux dans les entreprises visitées et des outils de formation et d'aide à la gestion des ÉPI pourraient être aidants à cet effet. Il est également soupçonné que le lavage des mains pourrait contribuer fortement à une diminution de l'absorption cutanée (Hou et al. 2016), mais cela demeure un aspect important à vérifier.

L'absence de données exhaustives sur la toxicité est un obstacle à l'établissement de valeurs limites d'exposition professionnelle. Par conséquent, cette recherche devrait encourager la réalisation d'études sur la toxicité endocrinienne des ignifuges. Une méta-analyse sur les associations entre les PBDE et les hormones thyroïdiennes pourrait s'avérer utile pour se prononcer sur la présence ou l'absence de lien entre l'exposition et cet effet sanitaire. Quant aux hormones sexuelles, plus de données seraient nécessaires pour corroborer les associations que nous avons observées. De plus, la compréhension des voies d'absorption privilégiées des ignifuges, à la fois dans l'environnement domestique et professionnel, est essentielle à l'établissement de mesures protectrices pour la population générale et les travailleurs. En ce sens, l'analyse de la distribution particulaire des différentes substances est également importante, ce qui informe sur les éléments les plus susceptibles de se retrouver dans la phase inhalable ou encore respirable.

Les données recueillies dans le cadre du projet IRSST et celles spécifiques à cette recherche serviront également à rédiger d'autres articles, pour lesquels la doctorante participe à l'analyse et à la rédaction. Les publications suivantes sont ainsi en cours de préparation ou en cours de rédaction, ce qui contribuera à étoffer les connaissances sur l'industrie du recyclage électronique :

- Analyse qualitative des pratiques de gestion de la santé et de la sécurité du travail dans le recyclage électronique (*Electronic Recycling Plants: Human Resources and OHS Management*, soumis à International Journal of Workplace Health Management) : Sylvie Gravel, Stéphanie Gladu, Daniel Côté, France Labrèche, Sabrina Gravel, Bouchra Bakhiyi, Joseph Zayed.;
- Évaluation de l'association entre les mesures dans l'air des OPE et les métabolites urinaires correspondants (en rédaction);
- Description des pratiques de santé et de sécurité du travail et exposition aux métaux dans le recyclage électronique (en rédaction);
- Évaluation de l'association entre les mesures dans l'air des PBDE et leur mesure dans le sang (en préparation);

7.6. Conclusion

Les ignifuges sont omniprésents dans l'environnement, les domiciles et les milieux de travail. Ces substances sont soupçonnées avoir un effet sur les niveaux d'hormones, ce qui est difficile à mettre en évidence. L'objectif de cette thèse était d'évaluer l'exposition à des ignifuges chez les travailleurs et d'étudier les effets endocriniens associés. Nous avons constaté que les travailleurs, et plus particulièrement les travailleurs du recyclage électronique, étaient exposés à des concentrations relativement élevées d'ignifuges. Le décaBDE est la principale substance mesurée, mais on note une multi-exposition à des ignifuges de plusieurs groupes chimiques, de même qu'à des métaux. De plus, des associations entre les concentrations biologiques d'ignifuges et les hormones sexuelles et thyroïdiennes ont été observées, dont certaines mises en évidence pour la première fois. Des efforts devraient être déployés afin de mieux comprendre ces associations, tout en diminuant les expositions dans ce milieu de travail en pleine expansion, le tout dans une perspective de prévention.

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Annexes

Annexe 1: Certificat éthique

Université de Montréal

Comité d'éthique de la recherche en santé

28 mars 2017

Objet: Approbation éthique – « Évaluation de l'exposition aux contaminants chimiques des travailleurs du recyclage primaire des matières résiduelles électroniques au Québec et appréciation du risque sanitaire. »

Mme France Labrèche, M. Jérôme Lavoué, Mme Sabrina Gravel & M. Joseph Zayed,

Le Comité d'éthique de la recherche en santé (CERES) a étudié le projet de recherche susmentionné et a délivré le certificat d'éthique demandé suite à la satisfaction des exigences précédemment émises. Vous trouverez ci-joint une copie numérisée de votre certificat; copie également envoyée au Bureau Recherche-Développement-Valorisation.

Notez qu'il y apparaît une mention relative à un suivi annuel et que le certificat comporte une date de fin de validité. En effet, afin de répondre aux exigences éthiques en vigueur au Canada et à l'Université de Montréal, nous devons exercer un suivi annuel auprès des chercheurs et étudiants-chercheurs.

De manière à rendre ce processus le plus simple possible et afin d'en tirer pour tous le plus grand profit, nous avons élaboré un court questionnaire qui vous permettra à la fois de satisfaire aux exigences du suivi et de nous faire part de vos commentaires et de vos besoins en matière d'éthique en cours de recherche. Ce questionnaire de suivi devra être rempli annuellement jusqu'à la fin du projet et pourra nous être retourné par courriel. La validité de l'approbation éthique est conditionnelle à ce suivi. Sur réception du dernier rapport de suivi en fin de projet, votre dossier sera clos.

Il est entendu que cela ne modifie en rien l'obligation pour le chercheur, tel qu'indiqué sur le certificat d'éthique, de signaler au CERES tout incident grave dès qu'il survient ou de lui faire part de tout changement anticipé au protocole de recherche.

Nous vous prions d'agréer, Mesdames, Messieurs, l'expression de nos sentiments les meilleurs,

Dominique Langelier, présidente
Comité d'éthique de la recherche en santé (CERES)
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Comité d'éthique de la recherche en santé

CERTIFICAT D'APPROBATION ÉTHIQUE

Le Comité d'éthique de la recherche en santé (CERES), selon les procédures en vigueur, en vertu des documents qui lui ont été fournis, a examiné le projet de recherche suivant et conclu qu'il respecte les règles d'éthique énoncées dans la Politique sur la recherche avec des êtres humains *de l'Université de Montréal.*

Projet	
Titre du projet	**Évaluation de l'exposition aux contaminants chimiques des travailleurs du recyclage primaire des matières résiduelles électroniques au Québec et appréciation du risque sanitaire.**
Chercheurs requérants	**France Labrèche** [redacted] Professeure adjointe de clinique, École de santé publique - Département de santé environnementale et santé au travail **Joseph Zayed** [redacted] Professeur associé, École de santé publique - Département de santé environnementale et santé au travail **Sabrina Gravel** [redacted] Étudiante, École de santé publique - Département de santé environnementale et santé au travail **Jérôme Lavoué** (ND), professeur agrégé, École de santé publique - Département de santé environnementale et santé au travail
Autres collaborateurs:	Daniel Côté, Louis Patry, Marc-André Verner & Jacques Lavoie (UdeM), Sylvie Gravel (UQAM) & Brigitte Roberge (IRSST) Coordination du projet: Bouchra Bakhiyi
Financement	
Organisme	IRSST
Programme	Subvention de recherche concertée
Titre de l'octroi si différent	
Numéro d'octroi	2015-0083
Chercheur principal	
No de compte	

MODALITÉS D'APPLICATION

Tout changement anticipé au protocole de recherche doit être communiqué au CERES qui en évaluera l'impact au chapitre de l'éthique.

Toute interruption prématurée du projet ou tout incident grave doit être immédiatement signalé au CERES

Selon les règles universitaires en vigueur, un suivi annuel est minimalement exigé pour maintenir la validité de la présente approbation éthique, et ce, jusqu'à la fin du projet. Le questionnaire de suivi est disponible sur la page web du CERES.

[redacted]

Dominique Langelier, présidente Comité d'éthique de la recherche en santé Université de Montréal	**28 mars 2017** Date de délivrance	**1er avril 2018** Date de fin de validité

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